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The Journal will make an especial feature of the review of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgement of all matter sent will be made in the department of reviews.

Editor

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The Relationship of Certain Focal Infections to General Disease in Infants and Young Children*

By McKim Marriott, M.D., *St. Louis, Mo.*

DURING recent years, much evidence has accumulated to emphasize the importance of focal infections in the causation of general disease during infancy and childhood. We have gradually come to realize that certain conditions, which previously have been regarded as nutritional and metabolic in origin, are in reality the result of infection. Certain infections such as those in tonsils and adenoids, middle ear, chest, genito-urinary system, bones and skin, can usually be recognized without much difficulty, by anyone who conducts a systematic search. There are other locations, however, in which infections occur which are not so obvious: for example in the mastoid antra of infants and in the nasal accessory sinuses of infants and young children. Failure to recognize these infections or properly to appraise their importance has been due to the difficulties of examination, the frequent absence of local symptoms and the prevalent but erroneous belief that the mastoid cells of infants and the nasal accessory sinuses of young children are not sufficiently well developed to be the seat of infections or to be amenable to treatment.

The general effects of infection are largely dependent upon the nature of the infecting organism. Thus infections in the mastoid and nasal accessory sinuses may lead to such a variety of conditions as vomiting, diarrhea and failure to gain in weight in the case of infants; hemorrhagic and tubular nephritis, heart disease, chorea, malnutrition, asthma and cyclic vomiting in older children. The clinical picture of low grade sinus infection may simulate that of such widely different conditions as pulmonary tuberculosis, appendicitis, malaria or encephalitis. There is no group of conditions in which the diagnosis is more frequently missed or in which treatment is more satisfactory, once a correct diagnosis is established, than those in which the infections mentioned are responsible.

The pediatrician sees these conditions at their onset and it is his responsibility to make the diagnosis and see that such treatment is carried out as will prevent chronic disease in later life. Even during earliest infancy focal infections may occur which

(*From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

**Read before the American College of Physicians, Cleveland, Ohio, February 24, 1927.)

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cause systemic manifestations. We have encountered mastoid antrum infections in premature infants during the first few weeks of life, and definite sinus infections in infants during the first four months of life.

During infancy the chief problem of the pediatrician is that of nutrition. We now have a clear idea as to the nutritional requirements and digestive capacity of the infant and have learned that all of the requirements may be readily met by simple foods and, most important of all, we have learned that if an infant has been taking a suitable food in adequate amounts and is failing to thrive, or has developed vomiting and diarrhea, the food is not at fault and does not need to be changed. The essential thing is to determine the underlying cause of the symptoms and this will most likely be found to be infection, either within or without the gastro-intestinal tract, provided, of course, that anomalies or mechanical conditions such as congenital malformation of the heart, or pyloric or intestinal stenosis are excluded. Congenital anomalies are rare and usually recognized without difficulty. The infections must be sought out.

Infection occurring within the gastro-intestinal tract itself may be the cause of the difficulty as in the case of bacillary dysentery and such infections should be discovered and appropriately treated or else ruled out. It is equally important to seek for such parenteral infections as we know are likely to be etiological factors in bringing about gastro-intestinal and nutritional disturbances. Infections of the middle ear are most common during early infancy. In most instances otitis media is readily recognized if one carefully examines the tympanic membrane. In other instances it is not so easy, particularly in the case of malnourished infants who have failed to thrive for a long time. The drum membrane may be neither red nor bulging, but careful observation with the electric otoscope may reveal a lack of luster and transparency. Paracentesis in such a case may be followed by the discharge of only a small amount of serum or a larger amount of pus. In a certain number of instances paracentesis is followed by improvement in the infant's general condition irrespective of any change in the character of the diet. Such happy results are, however, not always obtained. Severe diarrhea may continue or the infant may fail to thrive. In these cases, after other sources of infection have been searched for and ruled out, one should consider a possible infection of the mastoid antrum. Such infections are much more common than has been previously realized.

During early infancy the antrum and middle ear form essentially one cavity, communicating through the narrow *aditus ad antrum*. The antrum is the only mastoid cell developed at an early age and is a small cavity no larger than a pea. In middle ear infections the antrum is probably involved in most instances. When the middle ear is drained the antrum also drains unless obstruction occurs at the aditus. Such obstruction is not uncommon in infancy, as the aditus is narrow and the mucosa readily swells so as to completely shut off the antrum from the tympanic cavity. In these instances the infection remains in the

antrum and gives rise to constitutional manifestations. A walled-off infection in the antrum in the majority of instances does not lead to any local evidences over the mastoid region. There may be no redness, edema or apparent tenderness. The only local sign may be a sagging of the posterior superior canal wall just external to the tympanic membrane. This sag is due to the fact that the bony annulus is not complete so that pressure from within the antrum causes a protrusion of the canal wall. At times the sag may be so slight as to be hardly discernible. It is, in most instances, not recognized unless one is particularly looking for it and is using the electric otoscope.

The decision to drain the antrum rests on the pediatric as well as otologic considerations. The general symptoms depend to a certain extent upon the nature of the infecting organism and are not proportional to the degree of temperature reaction. We have observed epidemics of mastoiditis in infants, due to certain strains of hemolytic streptococcus, in which the symptoms were of a fairly uniform type and consisted of fever, diarrhea of the cholera infantum type, associated with dehydration and hydrolability, whereas other infants with mastoid infection of equal severity and, at times, with higher temperature showed neither vomiting nor diarrhea when the infecting organism was of a different type. The streptococcus, however, is not the only organism capable of bringing about severe diarrhea, although it is perhaps the most important. Members of the colon group and certain types of pneumococcus as well as other organisms have, in individual cases, led to severe diarrhea. On the other hand, there are strains of streptococci as well as other organisms which, when present in the mastoid antrum, lead to no very violent symptoms, but only to a slow but progressive loss in weight, occasional vomiting and ultimately to a condition of athrepsia or marasmus. In these cases there may be little or no fever but the blood leucocyte count is invariably elevated. Infections of the mastoid antrum which are acute in nature and lead to definite subperiosteal swelling rarely lead to the constitutional manifestations mentioned above and recovery in this latter group after operation is usually prompt.

When no other explanation for the symptoms is present and especially if there are otological evidences of antrum infection, the antrum should be drained. The operation, as performed in our clinic, has been described by Alden and Lyman (1). Local anesthesia only is used and a small button of bone over the antrum is removed and a gauze wick inserted. There is no appreciable shock and, in our experience, no mortality referable to the operation *per se*. We refer to this simple operation as "post-auricular drainage" or "antrotomy" rather than mastoidectomy. In most instances it is advisable to do post-auricular drainage on both sides, for bilateral infection is the rule. This simple operation has, in our experience, given most gratifying results, especially when done early and before the infant is in critical condition. Many of our worst cases of diarrhea, vomiting and severe nutritional disturbances

have responded promptly with marked improvement and ultimate recovery. It has been our custom to make no changes in the character of the feeding in these cases.

To give some idea of the frequency of these infections, there were recently 32 infants under two years of age in the wards of the St. Louis Children's Hospital; of these 28 had had antrotomies, ond in each instance definite infection in the mastoid antrum was discovered at the time of operation. It is during infancy that walled off mastoid antrum infections are especially likely to occur because of the anatomical considerations already mentioned.

As far back as 1684 Du Verney (2) recognized the presence of pus in the mastoid antra of young infants. It has been generally recognized for a number of years that nutritional and gastro-intestinal disturbances during infancy may be the result of infections in the middle ear. This point of view was clearly expressed by Hartmann (3) in 1898. Maurice Renaud (4) seems to have been one of the first observers to attribute nutritional disturbances in infants to infections of the mastoid antrum. Renaud based his conclusions on autopsy findings and on the beneficial effects of antrotomy. Byfield (5) and Floyd (6) working in conjunction with Dean of Iowa City have reported on cases of masked mastoiditis in early infancy in which excellent results were obtained following operation. Our own work on this subject was begun in 1923 when we discovered mastoid antrum infections at autopsy in the case of infants dying from severe nutritional disturbances. Following this finding a number of mastoid antra were opened during life and found to be infected and there was subsequent improvement in the general condition of the infants.

Certain nasal accessory sinuses are present, although small, even in early infancy. The maxillary antra are present, membranous sphenoids and some of the ethmoid cells. As the child grows, all of the sinuses enlarge and the frontal sinuses are ultimately developed. Sinus infection can occur at any age, and give rise to general symptoms. The diagnosis is difficult but possible even on very young children.

Direct rhinoscopic examination with a proper light is the surest method of detecting the local condition. In some instances it is advisable to conduct the examination under anesthesia with the use of the naso-pharyngoscope. The observation of pus coming from any of the sinuses of course makes the diagnosis evident, but it should be emphasized that the visualization of free pus is not essential for the diagnosis of chronic sinus infection. There may be merely reddening and swelling around the ostea or a slight serous exudate. In the case of maxillary sinusitis, the diagnosis may be confirmed by irrigation and culture of the material removed. Local symptoms of pain and nasal discharge are not necessarily present, but enlargement of the cervical glands, especially of the posterior chains is a constant finding.

Transillumination of the sinuses is of relatively little value as a means of diagnosis. The X-ray is of much greater value but this, too, is at times

untrustworthy. Lack of development of one or more sinuses, particularly of the frontals as revealed by roentgenography is indicative of long standing infection.

One of the most frequent general manifestations of chronic sinus infection in children is a picture simulating that of tuberculosis. The child is pale, languid, has slight evening temperature and often a chronic cough. X-ray of the chest in these cases shows an enlarged hilus shadow and peribronchial thickening, often extending well out into the parenchyma of both lungs. Small dense areas such as are usually interpreted as shadows of calcified glands may be seen. Tuberculosis in these cases may be ruled out by negative intradermal tuberculin tests using increasing amounts of tuberculin. Successful treatment of paranasal sinus infection in these cases results in marked and progressive improvement.

Other symptoms which we have often observed associated with chronic sinus infection have been repeated attacks of abdominal pain, often accompanied by vomiting. In some of these patients the symptoms have been so suggestive of appendicitis that the abdomen has been opened but no pathological conditions found. except in certain instances enlarged abdominal glands. Brenneman (7) has drawn attention to the association of such abdominal attacks with throat infections. Chronic digestive disturbance associated with achlorhydria is another manifestation of chronic sinus infection.

Asthmatic symptoms are observed in children suffering from chronic sinus infections. When asthma is due to definite sensitization, there occurs a hypertrophic condition of the nasal mucosa which is said to predispose to sinus infection. In other instances, however, the sinus infection is apparently the original cause of the asthma.

Children with chronic sinus infections, especially those who are also malnourished, are likely to develop heart murmurs and a certain degree of cardiac dilatation. The erroneous diagnosis of organic heart disease is often made on these patients, but the disappearance of the murmurs and the return of the heart to normal size following the removal of the infection and improvement of the general nutrition speak against the probability of valvular endocarditis. On the other hand, sinus infection is usually observed in patients having true rheumatic endocarditis and the other rheumatic manifestations of chorea and articular rheumatism. In this rheumatic group the sinus infections have not usually been accompanied by the presence of thick pus, but there has been a thin serous pus found in the sinuses, especially the maxillary antra and in addition in those cases which have been operated upon radically a tremendous amount of granulation tissue has been found. In our experience, clearing up of sinus infections has been more effective in preventing recurrence of chorea, rheumatism or endocarditis than has the mere removal of tonsils and adenoids.

The association of chronic arthritis with focal infections is, of course, well recognized.

One of the most important and clear cut of the manifestations of infection in the nose and throat is ne-

phritis. The two common forms of nephritis occurring in childhood, namely tubular nephritis or "nephrosis" and glomerular or "hemorrhagic" nephritis have, in our experience, invariably been associated with infection. The infection has been found more frequently in the nose and throat than elsewhere in the body. The characteristics of tubular nephritis or nephrosis are the passage of scanty amounts of urine containing large amounts of albumin and numerous casts but no blood, normal phenolsulphonephthalein output, no retention of non-protein nitrogen and no elevation in blood pressure; marked generalized edema and ascites and severe anemia. Clausen, (8) working on cases of nephrosis in the St. Louis Children's Hospital, pointed out the association of these cases with infections of the paranasal sinuses, especially the maxillary antra. The infecting organism has most frequently been a hemolytic staphylococcus. Clausen (9) demonstrated the presence in the blood and urine of a substance having a marked physico-chemical effect and capable of altering the permeability of membranes. This substance disappears from the blood and urine coincident with a clearing up of the sinus infection and subsequent disappearance of the edema. The effect of suitable treatment has been truly remarkable in these cases of nephrosis. Thus we have observed a young child to lose as much as 15 pounds of fluid within five days time, following the drainage of infected sinuses. When the sinus infections have been satisfactorily cleared up, complete disappearance of the albumin from the urine is the rule. We have examined a number of these patients at intervals for several years afterwards and have found no remaining evidence of nephritis. Re-infection of the sinuses may, however, cause a return of all the symptoms. Infections which have persisted for a long while sometimes lead to permanent changes in the kidneys, but complete recovery is possible in the case of uncomplicated tubular nephritis. Unfortunately it is not always possible to completely eradicate the infection but this is the only method of treatment which is calculated to bring about more than temporary or symptomatic improvement. Dietary regulation, restriction of fluid, sweating, purging and the use of diuretics are methods of treatment capable of accomplishing no permanent improvement. Recovery following the use of such methods is to be attributed to spontaneous clearing up of the infection in the sinuses or elsewhere.

Hemorrhagic or glomerular nephritis is usually, if not always, the result of a streptococcus infection. The most common causes of such a nephritis are streptococcus infections of the nose and throat, including the scarlatinal infections. The streptococcus is more likely to invade the tonsils, adenoids, middle ears and mastoid than the nasal accessory sinuses. In glomerular nephritis, in distinction to nephrosis, there is blood in the urine at some stage, the urine is not necessarily scanty, retention of non-protein nitrogen occurs in the blood and in cases of long standing some degree of hypertension is the rule. There are also changes in the capillaries throughout the body. In the majority of in-

stances, hemorrhagic nephritis is of short duration and clears spontaneously. If, however, the infection persists for a considerable length of time permanent damage to the capillaries of the renal glomeruli occurs and then, even though the source of infection is subsequently removed, complete recovery is not possible.

The conditions so far mentioned are those of fairly common occurrence. Occasionally certain bizarre symptoms referable to sinus infection are observed. Thus we have seen three patients whose symptoms simulated epidemic encephalitis. We have observed in different patients hemiplegia, paraplegia and a symptom complex referable to extra-pyramidal lesions in which the association with sinus infection was definitely established. We have also observed children whose symptoms were indistinguishable from idiopathic epilepsy in whom the manifestations have ceased following the successful treatment of sinus infection.

The diagnosis of sinus infections in general must be made by the internist or pediatrician rather than by the otolaryngologist. It is the internist who first sees the patient and unless he recognizes the general symptoms indicative of local infection, the otolaryngologist will not be called. The diagnosis of the individual sinuses involved is a problem for the otolaryngologist, but due to the fact that the importance of sinus infection in children has not until recently been sufficiently realized, consultations with otolaryngologists are often unsatisfactory. Infinite patience and special technic are necessary if a correct diagnosis is to be made and unfortunately otolaryngologists have centered their attention on tonsils, adenoids, and obvious mastoid infections to such an extent as to practically ignore the sinuses.

In the majority of instances local treatment, possibly with irrigation of the antra, is all that is necessary to bring about satisfactory results. The treatment as outlined by Arbuckle of this clinic has been most satisfactory. This consists in irrigation with a 10% solution of glucose (Cerelose) once or twice daily, followed by oil of rose sprays and the instillation of a weak mercurochrome solution of 0.3 to 0.5%. During the irrigation with the hypertonic glucose solution the head must be held forward and down. When the mercurochrome drops are instilled the child lies on the back with the head over the edge of the bed. Ephedrine instillations leading to a shrinkage of the nasal mucosa result in better drainage and tend to aid in bringing about a clearing of the infection.

In the presence of badly infected tonsils and adenoids, these should be removed. In some cases it is necessary to cut windows in the maxillary sinuses in order to bring about adequate drainage and ventilation.

In a few instances it becomes necessary to perform radical operations upon the upper nasal sinuses. In general, operation during the acute stage, especially of streptococcus infections, is to be avoided. The time for operation is during the subacute or chronic stage of the infection.

From what has been said, it must not be assumed that every infant with

vomiting and diarrhea or every child suffering from any of the manifestations mentioned should immediately be subjected to treatment operative or otherwise of the mastoid or nasal accessory sinuses. We do not wish to overemphasize the importance of these infections, but merely to draw attention to the fact that such infections are too often overlooked as possible factors in the causation of general symptoms. It is admitted that sinus infections are frequent in children who show none of the symptoms mentioned and also that during almost any bad "cold in the head" there may occur some sinus infection. There is, however, a large group of cases in which an etiological relationship between sinus infection and general disease manifestations is so evident as to leave little doubt in the mind of the observer.

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Mucous Colitis (Colonic Vagotonia)*

By John Dudley Dunham, A.B., M.D., *Columbus, Ohio*

THE synonyms by which this disease is known are numerous and confusing. Writers have used the terms: Myxorrhea coli, muco-membranous colitis, myxoneurosis intestinalis membranacea, hypochondriasis pituitosa, catarrhal colitis, and chronic intestinal catarrh, most of which are misnomers.

The few necropsies (1) performed on patients dead of this disease when uncomplicated reveal no evidence of an inflammation of the large bowel.

Hence, colitis conveys a very erroneous conception. Cabot's (2) suggestion "colica mucosa" is better, though the part affected is not mentioned.

Colonic vagotonia covers the part involved as well as the etiologic factor.

The first description of this disease has a very ancient origin. It is to be found in II Chronicles, Chapter 21, verses 12-19 inclusive:

12 'And there came a writing to him (Jehoram), from Elijah, the prophet, saying, Thus saith the Lord God of David thy father, Because thou hast not walked in the ways of Jehoshaphat thy father, nor in the ways of Asa, king of Judah,

15 Thou shalt have great sickness by disease of thy bowels, until thy bowels fall out by reason of the sickness day by day.

18 And after all this the Lord smote him in his bowels with an incurable disease.

19 And it came to pass, that in process of time, after the end of two years, his bowels fell out by reason of his sickness, so he died of sore diseases.'

This was probably a case of mucous colitis. The powerful suggestion made through Elijah doubtless caused him to scrutinize his stools. Then arose the diarrhoea with mucous casts. The emotional state of the ancient king must have been distressing, causing his vagotonia and perhaps sitophobia and starvation. This patriarch was stricken at the early age of 38 and succumbed within 2 years. Had the Lord seen fit to revise his prophecy the altered emotional state of Jehoram might have released the hypertonicity of his vagus.

If our diagnosis is correct, the patient would then have been allowed to fulfill the allotted span of three score years and ten (3).

The scientific discussion dates at least to Paulus Aegineta in the early period of the seventh century, who considered the entity as a discharge of the inner coat of the bowel.

*Read at the Eleventh Annual Clinical Session of The American College of Physicians, Cleveland, Ohio, February 21, 1927.

ETIOLOGY

Opinions about causation are as various as there are observers who have reported cases.

A preponderance of certain types of bacteria in the intestinal flora has been insisted upon by some clinicians as the sole factor.

Cabot (2) states that colica mucosa is a form of neurosis associated with constipation, recurrent attacks of diarrhoea and sometimes with starvation.

W. S. Thayer in a discussion of the above paper holds that "a nervous element is an associated element and is not the cause of mucous colitis."

Thus do the masters disagree.

Norman (4) contends that McCarrison's studies suggest a deficiency of Vitamin C with an excess of starches, or starches and fats, which produces pathologic lesions in the intestinal tract similar to those in mucous colitis. Further "mucous colitis must be considered as the most manifest part of a general constitutional disorder brought about chiefly through dietary deficiencies and excesses and the occurrence of other infections."

Goldman's (5) discussion of etiology holds that "the condition may be brought about by abnormal endocrine function, infection of the intestines from focal lesions in the teeth, tonsils, appendix, or gall bladder, from ptomaine or chemical poisoning, from mechanical obstruction, and from faulty metabolism."

J. M. Da Costa (6) was apparently the first to suggest the true conception of this disease as a dyscrasia of the vegetative nervous system. He said, "It is doubtful if we can consider the affection as originally an inflammation at all. Is not the true trouble in the nervous system in the nerves presiding over secretion and nutrition in the abdominal viscera?

Chas. L. Mix (7) and B. L. Spitzig (8) have very clearly defined mucous colitis as a Vagotony.

The effect produced upon the unstriped muscle of the alimentary tract through emotional states offers, to my mind, the only satisfactory explanation of mucous colitis. Worries, marital infelicities, unsatisfactory sexual relations all have a tendency to produce this disease.

Judge Lindsay's suggestion of companionate marriage would reduce the frequency of colonic vagotonia in young women.

No more classical or accurate clinical description of this disease has been written since Da Costa's article published fifty-five years ago. (6)

"The disease is characterized, as already said, by attacks of abdominal pain, followed by the discharge of what looks like skins or membranes, sometimes coming off in the shape of moulds or long tubes. There may be but one attack; but this is very exceptional, much more generally one paroxysm is followed after an interval of months by another, and yet another; and at times the disease may become almost continuous, with occasional distinct exacerbations. A week, in my experience, is the shortest time for an attack to last, and distention, sense of burning, colicky pains and at times a sluggish state of the bowels, precede the discharge by days. After this has taken place, the abdominal soreness lessens, the feeling of raw-

ness passes off, and the patient is well, though he is apt to have a coated, flabby tongue, to remain dyspeptic, and be readily fatigued. If he has lost flesh during the seizure, he regains it entirely, or to a great extent, and, at no time, unless in an aggravated case, does he emaciate much. From the history of the ailment and the amount of abdominal soreness during the attack, we might expect febrile phenomena, but the skin is prone to be cool, the hands and feet are often moist and clammy, and the circulation feeble and languid. Palpitation, particularly of the abdominal aorta, is common. Between the attacks, the bowels are irregular, sometimes constipated, at others loose; and tenesmus is often complained of. The patient suffers from sore mouth, from papular eruptions, from boils, or even carbuncles; he has an unhealthy complexion, and *almost invariably exhibits some signs of his nervous system being disordered*. His bladder sympathizes in the intestinal derangement; it is irritable, and we have not unfrequently observed that large quantities of mucus are passed. All these symptoms come out in bold relief, during an attack, but in a slight form they may be noticed in the interval. After a few seizures the patient may gradually recover, yet is never robust, or the disorder becomes persistent. I repeat that in the rarest of instances only is it a short one."

DIAGNOSIS

Patients usually consult a physician with the diagnosis ready made in a specimen bottle. The tendency to introspection and constant observation of the stool is almost universal.

To avoid error the stool should be carefully examined to eliminate particles of food, intestinal parasites and the evidences of actual colitis with ulceration.

If you find blood in the stool you are not dealing with colonic vagotonia.

The physician may be misled by the character of the pain and soreness into a diagnosis of peptic ulcer, cholecystitis, or appendicitis.

Operations upon patients with mucous colitis are much less frequent than in former years.

Surgeons have learned to be very sceptical about diagnoses of supposed abdominal lesions when patients have psychasthenia or hypochondriasis.

Every patient in whom there is a suspicion of colonic vagotonia should have a sigmoidoscopy performed as well as a fluoroscopic observation, of a barium meal. The latter procedure will reveal the phenomenon of spasticity which is an essential occurrence.

Mild cases without colic are most frequently overlooked and treated for hyperchlorhydria, neurasthenia, etc.

Thoughtful clinicians realize the wide spread occurrence of this type of disease.

TREATMENT

A perusal of the literature in recent years presents the most varied suggestions from capable internists.

One finds the extremes of a roughage diet and a very bland diet recommended. Some insist upon repeated colonic irrigations, apparently to free the bowel of mucus, while others advise against any local interference with the gut.

Luginbuhl (9) very aptly remarks that "colitis is no exception to the general rule that treatment should be directed to the cause, rather than to the suppression of the effect."

With many others he strongly disapproves of irritant cathartics and copious flushings of the bowel.

A bland non-irritating, nourishing diet has an appeal as a rational procedure in these cases. If the patient can add 10 or 20 pounds to his weight improvement is aided.

If one accepts the well established theory that true mucous colitis is caused by a disturbance of the emotions with a resultant hypertonicity there should be no question as to treatment.

A careful analysis of the patient's mental state and pyschic shocks is fundamental.

This usually cannot be determined at one consultation and often only after a protracted period in which the confidence of the patient is secured.

Personally, I have never seen this disease in other than psychoneurasthenics or hypochondriacal individuals.

After the nature of the abnormal emotional state is discovered, the physician must use suggestion and also attempt to change the patient's attitude toward his life.

Re-education for the purpose of drawing his attention away from the bodily functions is a sine qua non.

This can never be done by drugs, colonic irrigations, or close attention to diet. Belladonna is the only drug which I have found beneficial. The more rectal injections the longer you will treat the patient.

Those who have recognized many cases of colonic vagotonia will realize that the treatment is not along a flowery path.

Unless the patient can be made to understand that he has no serious organic disease and that his disorder is curable largely by his own efforts, your psychotherapy will be unavailing.

Without the above management of your patient, autogenous vaccines, colonic irrigations, drugs, cathartics, and even implantation of *B. Acidophilus* will not cure the disease. Improvement by these latter means must be explained upon the theory of suggestion.

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Treatment of Carcinoma of Rectum by Radium*

(Presentation of Case)

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While we feel at the present time that whenever possible the best treatment for cancer of the rectum is some type of radical operation, there remain two classes of patients to whom we must offer some alternative treatment: first, those who are in an inoperable condition; and second, those who refuse the radical operation. There are a considerable number in the latter class who must command our attention, for if we do not offer another therapeutic measure they will immediately become the prey of quacks. We have therefore resorted to the use of radium in the treatment of these two classes of cases and wish to report our results in a series of 65 cases.

Radium has certainly established its value in the treatment of epithelioma of the skin, lip and tongue and of cancer of the antrum and cervix, but its use has been more limited in the rectum, and we shall have to have more statistical information and better results than have been obtained in the past before this field will be yielded to radiation therapy, as has happened in the case of cancer of the cervix. Although it is true that surgical results have not been excellent in the past, I believe that the surgical treatment of cancer of the rectum will improve in the future and will show a greater percentage of cures, so that radiation therapy will also have to advance in order to compete with surgery.

With the possible exception of cancer of the esophagus, cancer of the rectum is one of the most difficult diseases to treat successfully, chiefly because of its inaccessibility. Most malignancies are quite easy of access, at least as compared with cancer of the rectum. I would also call your attention to the difficulty encountered in the treatment of cancer of any organ which is physiologically functioning for the well-being of the patient, such as the esophagus, the stomach, the bladder, or the rectum. In the treatment of other organs such as the uterus, on the other hand, there is no particular physiological function to be provided for, the radium can be applied more easily, the dose can be larger, and all of these factors aid in securing better results.

In the treatment of cancer of the

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rectum we advise a colostomy preliminary to the radium treatment—the incision being made large enough to permit an exploration for the purpose of determining the condition of the liver, the mesenteric glands, and the peritoneum in the floor of the pelvis, for obviously if these are grossly involved the patient should not be subjected to treatment which will not benefit him. Colostomy greatly minimizes the discomfort of the patient during the period of reaction to the radium treatment, and while in the past some cases have been treated without colostomy, at the present time we insist on it.

After the colostomy has been made the distal segment of the colon is irrigated daily with large quantities of water to insure absolute cleanliness, for in the presence of infection the reaction to the radium is likely to be quite severe. The radium treatment is given about seven days after the colostomy has begun to function satisfactorily.

The technique of the application of radium differs somewhat with the nature of the lesion. If it is papillary in nature, needles or emanation tubes may be placed throughout the growth. If there is a large flat ulceration, an oval flat applicator can be made with radium tubes evenly distributed throughout. If there is a narrow constriction, tubes can be placed in tandem in a rubber tube and directed into the lumen of the bowel. It is very essential that the radium be placed accurately in proximity to the growth and we recommend that the procedure be carried out under sacral anesthesia without moving the patient from his bed. If one gives a general anesthetic or moves the patient after treatment the radium is quite likely to be displaced.

The dosage varies with the size of the growth. In our cases the dosage has varied from two to three thousand mg. hours, the average being 2600 mg. hours. Two treatments are generally given about three hours apart. In one case, however, in which a papillary growth had extended to the buttock and vagina, over five thousand milligram hours were used. We employ a 1½ mm. brass screen the thickness of a rubber tube, which is about 3 mm. When the radium reaction has subsided the patients are given external radiation by x-ray. According to our experience, further radiation after the initial course is of little value. If recurrence takes place it is treated by the implantation of a few seeds in the area, but a large amount of radium is not needed and should not be used, for it is quite apt to produce excessive pain. If after one and one-half or two years there is no evidence of disease, and the bowel is not constricted, then if the patient insists, the colostomy may be closed. This has been done in two of our cases.

Complications: The chief immediate complication of treatment with radium is pain and a bearing-down sensation and these, if severe, combined with loss of sleep wear out the patient very quickly. These symptoms are due to the intense in-

flammatory reaction and generally begin about 10 days after the radium has been applied. The amount of the discomfort is generally proportionate to the area of normal mucous membrane which has been affected, so that it is necessary to protect this as much as possible, and therefore whenever it is possible, I insert a lead plaque 2 mm. thick between the radium tubes and the healthy mucosa. Olive oil enemas and suppositories are of some help in relieving the discomfort. Often in about three or four weeks after the treatment these patients complain bitterly of hemorrhoids. This is due to thrombosis in the hemorrhoidal veins and the ensuing congestion lower down. If there is thrombosis of the external veins it can be relieved by turning out the clot.

In all cases in which a colostomy has been made through and through irrigation is carried out, for cleanliness is of great aid. The closer the growth is to the sphincter the more severe the pain, therefore in such cases I perform a subcutaneous myotomy on the sphincter ani, using much the same technic as is used in making a subcutaneous tenotomy. This greatly relieves the terrific spasms of pain. The advantage of making the myotomy subcutaneously about an inch from the anus is that no raw surface is left at the muco-cutaneous junction, which in itself would be painful on account of the irritating discharge, and might heal with difficulty.

The later complications that appear are stricture of the rectum and metastases. We know that in the healing process a great deal of scar tissue is produced, which later contracts and often almost completely obliterates the lumen, but this is not necessarily serious if we have been fortunate enough to eradicate the disease. It does, however, complicate the closure of the colostomy. We have several cases in which the colostomy could be closed except for this complication. I am contemplating trying out the carbon dioxid snow treatment for these strictures, but whether or not this would have the same effect as in benign strictures I am unable as yet to say.

Metastasis into the pelvic glands is generally evidenced by pain deep in the pelvis and hip and referred down the leg. When this occurs further x-ray treatment may be tried but radium is not advised. If the primary growth was in the distal inch and a half of the rectum, such extension is by the inguinal glands; and if they are present it is well worth while to remove them surgically. Extension into the liver occurs frequently and occasionally into the lungs, and for carcinoma in these organs treatment so far has not been successful.

Results: In our series of 65 cases of carcinoma of the rectum a colostomy was performed in 53; the other 12 patients refused to have a colostomy, and of these all except one are dead.

Approximately two-thirds—44—were in men and one-third—21—were in women. The average age of the men was 57, of the women 45. Thirty-nine of the men were

married and six single; 16 of the women were married and five single. The oldest patient in this series was a man, 74 years of age, the youngest a woman 25 years of age. An interesting feature of this series is the wide variation in the duration of symptoms before the patients came to us—these periods varying from one to 36 months, the average period being 12 months. A mistaken diagnosis, frequently of hemorrhoids, was usually the cause of this delay. We feel that these mistaken diagnoses are usually to be attributed to the custom of making a diagnosis without a digital examination.

That so many of these patients could go along for 36 months without serious difficulty can only be explained by the fact that cancer is variable in its attack on different individuals. One cannot base a prognosis on information gained from mass statistics, for no two cases behave the same. This point is well illustrated by one of our cases of carcinoma of the cervix, in which the patient had had the growth for 11 years and had received no treatment. Before we examined her we were reluctant to believe that the growth could be a cancer, but the diagnosis was confirmed by a microscopic examination. In some cases patients with cancer of the breast also remain untreated for many years without any ill result. In like manner the course of rectal carcinoma varies with the individual.

Of the 65 cases in our series 57 were inoperable and eight were operable. Of the eight operable cases, six patients are living and two are dead; and among the six who are living the duration of life to the present time has been from two to four years. Of the 57 inoperable cases, eight of the patients are living and 49 are dead; among the eight patients who are living, the duration of life has been from two to four years. The average duration of life among these eight living patients has been 35 months, and they have all been able to resume their regular occupations.

One case in this series deserves particular mention:—The patient was a man 68 years of age when he first came to us, four years ago. At that time he had a carcinoma of the lower portion of the rectum, near the sphincter. A colostomy was done on February 27, 1923, and radium was applied one week later. The lesion healed very well and at the end of 15 months the colostomy was closed. In March, 1925, 25 months after the primary lesion was treated, a metastasis developed in the left inguinal glands. The glands were excised on both sides and ten days later the right and left inguinal regions were treated by x-ray. The excision was followed by transient elephantiasis of the penis and the scrotum but there have been no other ill effects. It is now two years since the inguinal glands were removed and over four years since the carcinoma of the rectum was treated, and the patient is perfectly well. Cases such as this prove that one cannot foretell what the results of treatment may be.

General Discussion of Diseases of the Spleen*

By JOHN TUCKER, M.D., *Cleveland Clinic, Cleveland, Ohio*

BEFORE entering upon a discussion of certain pathological conditions of the body which are produced wholly or in part by abnormal changes in the spleen we must consider certain aspects of the anatomy and physiology of this organ. The large size of both the splenic artery and vein demonstrates that this organ is important as a hematopoietic or hemolytic structure. It has been asserted that at birth about 20 per cent of the portal blood comes from the spleen and in disease even a larger percentage of the hemo-fluid originates in this organ. As to its internal structure, we are particularly concerned with those large endothelioid cells which are present in the reticulum and pulp and which histologically have the power to take a vital stain. These great cells with single nuclei and clear cytoplasm are found not only in the spleen itself but also in the lymph nodes, in the adrenal cortex, in the hypophysis, as the Kupfer cells of the liver, as the Rouget cells of the capillaries and bone marrow, and as the endothelial cells of the body.

These characteristic cells, which are scattered so widely through the body, have been termed by Aschoff (1) the *reticulo-entdothelial system.* To them have been ascribed many functions which formerly were thought to be limited to the spleen. Therefore we would like to discuss the normal and pathological functions of the spleen not only as an organ *sui generis,* but as a member of this important and widespread system — the reticulo - endothelial system of Aschoff.

The many functions of the spleen which are known or which are supposed to exist are as follows:

I. The spleen is a reservoir for the red blood cells in the body. Reasonable proof of this storage function has been adducd by Prof. J. Barcroft (2). He shows by experiment that splenectomized guinea pigs die sooner in an atmosphere of pure coal gas than do guinea pigs with intact spleens. His explanation of this phenomenon is that when the red blood cells of the circulating blood are so saturated with carbon monoxid hemoglobin as seriously to impair the ability of the blood to supply oxygen to the tissues, then by its maximal contraction the spleen forces a quantity of normal red blood cells into the blood stream. Thus by giving a temporary fresh supply of oxy-

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hemoglobin to a splenectomized animal its life will be prolonged for a short time.

II. A second function indicated by the above experiment is that the spleen has the ability to expand and to contract—thus assisting in regulating the total volume of blood. By a second ingenious experiment Prof. Barcroft and his associates proved this point. He attached lead strips to different points in the splenic surface in cats and then by taking x-ray plates he demonstrated that the spleen varies greatly both in shape and size during different phases of digestion, and its size is reduced by exercise. He proved also that after the death of the animal the spleen may be only one-half the size of the resting spleen during life. If we are justified in applying these findings in animals to man, then we must admit that the spleen 'pulsates' and we must also recognize that in the living human subject its weight is more than that of the average spleen in the cadaver—195 gms. That is, during or shortly after the period of lethal exodus the size of the spleen is reduced by contraction.

III. The spleen increases the fragility of the red blood cells in the presence of hemolytic agents. Many workers have shown that the red cells of the splenic vein are less resistant to hypotonic salt solutions than are the red cells of the peripheral circulation. In 1918 Drs. Pearce, Krumbhaar and Frazier (3) concluded an important study on the effect of splenectomy in dogs. One of the facts established by these investigators was that after splenectomy the red blood cells show increased resistance to hemolytic substances such as hypotonic salt solutions, hemolytic serum, saponin, venom and mechanical agitation. In the presence of certain pathological changes in the spleen and reticulo-endothelial system—as in Banti's disease and familial hemolytic icterus, we have every reason to believe that this function of blood destruction is increased to pathological proportions with the resultant production of anemia and the overloading of the liver with bile pigments and toxic products of cellular degeneration by way of the splenic vein, these sequelae progressing to the ultimate production of jaundice and hepatic cirrhosis.

IV. As a corollary to the function of red blood cell destruction Mann and Sheard (4) of the Mayo Clinic have performed experiments which give certain evidence that the reticulo-endothelial cells of the spleen and elsewhere are able to form bile pigment from the iron-free moiety of hemoglobin, thus forming at least a part of the liver bile. During my own term as House Officer at Lakeside Hospital I was able to show that bile pigment could be formed from blood extravasated into various serous cavities of the body. This included the pleura, peritoneum, pericardium, subarachnoid space and synovial sacs of the knee. Whipple (5), also, has long since shown that bile pigment can be formed outside the liver.

V. A fifth function of the spleen is its ability to destroy blood platelets. The fact is now generally accepted that the presence of a sufficient number of blood platelets is essential to the formation of a normal *retractile* clot, and that if the platelets are insufficient in number or are absent, then the clot, even though it forms in a normal period of time, will nevertheless be non-retractile, so that there is resultant predisposition to hemorrhage.

In this discussion I wish to call your especial attention to three of these functions which may reach harmful proportions when the spleen and reticulo-endothelial system are diseased—viz. the destruction of red blood cells, the destruction of blood platelets, and the sending of abnormal quantities of bile pigment and toxic products to the liver.

To illustrate these changes, I should like to discuss three types of diseases of the spleen and of the reticulo - endothelial system:—(1) Splenic anemia or Banti's disease; (2) hereditary splenomegalic hemolytic jaundice; and (3) thrombocytopenic purpura hemorrhagica. Each of these conditions represents a disturbance of one or more of the above functions of the reticulo-endothelial system.

Banti's disease—splenic anemia—is characterized by a progressive enlargement of the spleen, secondary anemia usually intermittent, a tendency to hemorrhages, especially those of gastric origin, esophageal varices, and later secondary cirrhosis of the liver with jaundice and ascites (Osler). Leucopenia is usually present. The disease is often divided into three periods: (a) enlargement of the spleen, (b) beginning congestion of the portal circulation, (c) cirrhosis with ascites. Pathologically there is marked fibrosis of the spleen with increased firmness in its texture and thickening of the capsule. Banti has found a proliferation of the endothelial cells of the venous sinuses of the pulp. This would correspond to the hyperplasia of the reticulo-endothelial system demonstrated by Aschoff.

Splenectomy gives the best results in the first stage, although cases of cure have been reported even after cirrhosis of the liver and ascites have developed.

It is very unusual for this disease to be seen in children. However, two of our cases were in children, one in a boy of 6 years and another in a boy of 7 years of age. Both had anemia, an enlarged spleen, gastric hemorrhages and leukopenia, but no cirrhosis or ascites. Both of these patients made a good recovery after splenectomy. Both children are living more than three years since the operation and while they are not robust they are in reasonably good health; the blood counts are over 4 million and there has been no recurrence of hemorrhages.

In a third case—that of a boy 19 years—the usual picture of splenic anemia was present. This patient made an exceptionally good recovery after splenectomy. His disease must have existed for fully 15 years, since he had had an en-

larged spleen and had vomited blood at the age of 4 years. Prior to operation an examination of his blood gave the following findings: —R. B. C., 1,650,000, W. B. C., 1300 and Hb., 30 per cent. A blood transfusion with splenectomy raised the cell count to R. B. C., 6,400,000, W. B. C., 17,800 and Hb., 75 per cent. While this patient was in the hospital a severe attack of streptococcic tonsillitis developed and the white blood cell count rose to 25,000, but he seemed to resist the infection very well and the acute phase of the tonsillitis subsided. Since that time he has had two recurrences of tonsillar inflammation but has resisted the infection very well with no material diminution in the red blood cells. The tonsils are still enlarged and there is a large lymph gland in the upper anterior triangle of the neck on either side. The patient's mother has repeatedly refused to permit a tonsillectomy—"So long as Bob is doing so well, I do not want him to risk another operation."

This last case brings out two interesting points:—(a) that the patient was able to tolerate splenic anemia for at least 15 years without the development of demonstrable cirrhosis of the liver and ascites; and (b) that he has been able to resist three attacks of tonsillitis and to carry septic tonsils without a recurrence of the anemia. This case together with several others in which infection has appeared in patients after removal of the spleen leads me to believe that splenectomy does not cause any lowering of resistance to infection. Certainly we are quite sure that after removal of the spleen the other portions of the reticulo-endothelial system undergo hyperplasia and if antibody formation occurs in this system then the patient is in better condition to resist infection after the diseased spleen is removed.

II. *Hereditary splenomegalic hemolytic jaundice,* first described by Munkowsky, presents a problem somewhat different from that presented by Banti's disease. The main characteristics of this syndrome as as follows:

The disease dates either from birth or begins in infancy or in early adolescence. The patient is continuously jaundiced but apparently is not ill. There is a chlorotic type of anemia—that is, there is a greater reduction in hemoglobin than in red blood corpuscles. The blood contains bile pigment but no salts and yet the urine is free from biliary elements. The presence of increased urobilin in the urine and stools indicates the abnormal blood destruction. The spleen is enlarged but the liver rarely extends much below the costal margin. The stools are normal in color. As a rule the red blood cells show increased fragility to hypotonic salt solutions. This condition may be hereditary but in such a case its course is similar to that of the acquired form. In the inherited type of the disease several members of the family are usually affected and the condition is probably handed down as a dominant Mendelian character.

Pathologically the spleen shows

marked engorgement and on microscopic examination the pulp seems to be crowded, while the sinuses are nearly empty. Gall-stones are present in about 60 per cent of the cases. There is a positive van den Bergh reaction from hemolytic icterus and the kidneys do not excrete the bile pigment.

The following case history will be cited in some details:

The patient, a little girl, 6 years of age, was presented with a questionable history of having had jaundice at birth. At the age of 2 years, however, the first frank appearance of jaundice occurred. Since then the skin had always been yellow with an underlying pallor. Exacerbations of the yellow color of the skin had been noted approximately every two months. The general health had been good save for a failure of appetite at the periods of icteric increase. There was no tendency to prolonged bleeding, no vomiting of blood, no nose-bleed and the urine had never been very dark in color. Occasionally the child had complained of a "hurting" in the stomach when awakening in the morning.

The *family history* was most important: the maternal grandmother, the great-grandfather, and an aunt had been habitually jaundiced. The mother also had been icteric and had had an enlarged spleen since childhood.

The *past history* of the patient included nothing of importance excepting a severe attack of measles in the preceding winter.

Physical examination gave normal findings except for a pale and icteric skin, some puffiness of the face, and slight jaundice of the sclera. The spleen could be palpated 4½ cm. below the costal margin in the anterior-axillary line, it descended on inspiration and showed a sharply defined border but no palpable notch. There was no enlargement of the lymph glands except in the upper anterior triangle of the neck on either side.

Laboratory tests gave the following findings:—Secondary anemia; increase in serum bilirubin; no bile pigment in the urine; normal platelet count; negative Wassermann test; and increased fragility in the red blood cells.

In summing up this case we find hereditary jaundice, increased bilirubin in the blood but no bile in the urine; an increase in the fragility of the red blood corpuscles; normal blood platelets; and pathological findings which confirm the clinical diagnosis. There was a striking increase in the red blood corpuscles 10 days after the operation, which was a long enough period to discount the effect of the one transfusion performed at the time of operation.

III. *Thrombocytopenic purpura hemorrhagic* is the most interesing disease of the group of diseases of the spleen and reticulo-endothelial system. In the majority of cases of this disease the results of splenectomy are quite dramatic unless the disease is of too long standing, on the one hand, or of the acute fulminating type, on the other. The important points in the diagnosis are the following:—

(a) An enlarged spleen is usually present.

(b) Bleeding from any part of the body such as the stomach, nose, gums, uterus, kidneys; petechias and ecchymosis of the skin.

(c) Prolonged bleeding time, due to a non-retractile clot, although the clotting time is normal.

(d) Positive capillary pressure determined by test with tourniquet applied for 5 minutes, as first described by Hess of New York City.

(e) Marked diminution or absence of blood platelets known as thrombocytes.

When such a syndrome is present we can expect splenectomy will result in a cure unless the remaining portions of the reticulo-endothelial system continue the abnormal destruction of platelets. Various workers have shown that in thrombocytopenic purpura the blood platelets are destroyed by the splenectomy. By examining the arterial and venous blood of the spleen, Myers, Waingot and Gordon demonstrated in one case that the splenic artery platelets were 325,000 and splenic vein platelets 65,000, thus showing a marked diminution in the number of thrombocytes leaving the spleen.

Microscopically the spleen shows marked proliferation of the endothelium and of the pulp sinuses and the lumina are stuffed with large cells.

Even though the cure which follows splenectomy in these cases is usually very dramatic, yet one of our patients who presented a typical picture of this syndrome failed to recover.

This patient was a white woman, 33 years of age, in whom during an attack of influenza petechiae developed on the extremities. Subsequent to this she remained pale and had recurrent subcutaneous hemorrhages, profuse menstrual flowing, attacks of fever and gradually increasing anemia. No enlargement of the spleen could be discovered by physical examination. However, the platelet count varied between 17,000 and 155,000 (normal 200,000 to 300,000), there was a non-retractile clot, fragility tests gave normal findings and the red blood cell count varied between 1,216,000 and 3,260,000. We had hoped that a blood culture would show streptococcus but none was found. The abnormal blood platelet destruction gave definite evidence of disease of the reticulo-endothelial system. Even though the spleen could not be palpated clinically it was removed, but no benefit resulted. It was apparent that the spleen was playing only a minor part in the disease. After three months in the hospital the patient was allowed to go home. A month later she died, but unfortunately no autopsy was performed.

We feel sure that this case should be classed as one of thrombocytopenic purpura hemorrhagica and that it was initiated by a so-called "influenzal" infection. However, we could not find any focus of infection, blood cultures were sterile and splenectomy resulted in no improvement.

Among these three types of splenic disease hemolytic icterus appears to be the only one that may be hereditary, although in several of our cases of Banti's disease we have obtained a history of the appearance of pallor

and of an enlarged spleen very early in life. I believe that the thrombocytopenic purpura is the result of infection, probably streptococcic in type, with localization of the organisms largely in the splenic portion of the reticulo-endothelial system.

Due to the very short time at my disposal I have refrained from discussing other diseases in which splenectomy may be indicated, such as abscesses, tumors, Gaucher's disease, splenomegaly associated with lues, tuberculosis, malaria, Hodgkin's disease, pernicious anemia, etc. Certainly splenectomy should be considered in any case of chronic disease in which splenomegaly is present and the patient has reached the dead level of chronic invalidism, and also even in cases of disease of the reticulo-endothelial system in which there may be no clinical evidence of enlargement of the spleen. However, under no circumstances save in a case of rupture by trauma or otherwise should the spleen be removed without a careful weighing of all the evidence secured from the history, from clinical examination and from laboratory tests.

CONCLUSIONS

The writer has presented this rather condensed paper concerning certain diseases of the spleen to show, first, that the spleen is not a useless organ; second, that it appears to have multiple important functions; third, that when enlarged it may be pathological; fourth, that in Banti's disease, thrombocytopenic purpura and hereditary hemolytic icterus we must make careful historical and clinical studies and tests before a differential diagnosis can be made; fifth, that splenectomy does not appear to lower the patient's resistance to infection; and finally, that acute infection undoubtedly plays a most important role in the diseases of the reticulo-endothelial system of Aschoff.

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Abuse of Iodin, Especially of Iodized Salt, in The Prevention of Goiter*

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IT may seem presumptious for me to attempt to discuss any phase of the relation of iodin to goiter at this time, when such an authority as Dr. Marine is to talk to you on the same subject, but my reason for doing so is that 15 percent of the total number of patients admitted to the Cleveland Clinic are goiter patients, and it is from the observation and study of this large group of cases that we have reached certain conclusions regarding the use of iodin in the various phases of this disease.

As the result of the extensive investigations by Marine and Kimball concerning the relation of iodin to simple goiter, and of those by Plummer and Boothby concerning its relation to hyperthyroidism, iodin has rightfully assumed a place of great importance in our therapeutic armamentarium. In the minds of many, however, its indiscriminate use is causing great apprehension, for the administration of iodin has been taken out of the hands of the physicians, who as a rule employ the necessary and recognized principles in selecting the cases suitable for its administration, and the public seems to have adopted for itself the dangerous principle that if everyone would take iodin goiter would automatically cease to exist. Two factors have been largely responsible for the general adoption of this idea by the public: first, the very great commercial possibilities which the manufacture of iodized products offers and the consequent wide-spread advertising of them; and second, the extreme gullibility of the public when it is a question of believing what it wants to believe. Particularly in this locality, where the goiter problem is so vital, the public is all too prone to accept such a simple solution.

It has long been a well known clinical fact that some people are more susceptible to iodin than are others, and that one of the dangers of the continued administration of iodin is the production of symptoms of hyperthyroidism. I doubt if any clinician who prescribes this drug routinely for goiter has not had a number of cases —and perhaps not a small number— in which the thyroid has become overactive. Dr. Crile, whose clinical experience with hyperthyroidism has been so extensive, has long felt that great care and judgment should be used when iodin is prescribed in cases of simple goiter, and that careful and frequent observation of the patient is the most important point of all.

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These conclusions were reached only after Dr. Crile had seen many cases of supposedly induced hyperthyroidism—I say supposedly, because clinical and experimental proof that iodin will induce hyperthyroidism cannot of course be presented, since this disease occurs so often in cases in which the etiological factors cannot be determined, and since attempts to produce it experimentally in animals have been unsuccessful. Our conclusions therefore must be based largely upon impressions gained from observation of the disease in large numbers of patients.

The most popular of the iodized products which have recently been offered to the public is table-salt with an iodin content of .02 percent. This is generally referred to as 'natural salt' on the supposition that this amount of iodin has been removed from the salt by the process of refining. Our attention was first attracted to this product in the summer of 1925, when quite a few unusual cases of hyperthyroidism in men were seen in the Clinic. The first one that especially attracted my attention was that of a postman who had had a large colloid adenomatous goiter for 20 years, but had always been well and had suffered no symptoms of hyperthyroidism until two weeks after he began the use of iodized salt. He was quite certain of the exact date upon which he began using the salt because his wife purchased it for the express purpose of curing his goiter. Two weeks later he began to lose weight rapidly and to feel extremely weak, and four weeks after beginning the use of the iodized salt he came to the Clinic complaining of 'paralysis' of the legs and of a loss of 14 pounds in weight. The supposed paralysis was nothing more than extreme weakness due to severe hyperthyroidism of which he showed all the characteristic signs except exophthalmos. His goiter had rapidly decreased in size during these four weeks and according to the patient the iodized salt was 'working wonders'.

In the following six months we saw a series of 50 cases of hyperthyroidism in men, all of whom had been using iodized salt. These cases were all marked by extreme weakness, particularly of the legs, and by loss of weight. In a large percentage of these cases no goiter was present nor had there been any goiter previously—there was also no exophthalmos in the majority of the cases. Perhaps I can best emphasize the unusual type of the disease in these cases by stating that many of these men had consulted one or more physicians before coming to the Clinic and that the nature of the disease had been unrecognized, whereas in this locality the ordinary type of hyperthyroidism is usually recognized very quickly. At the present time we have in the hospital a patient who works for a salt company in Michigan, who had consulted four physicians before coming to the Clinic. He was advised by the last two to have his appendix removed and he came here in the expectation that the diagnosis of chronic appendicitis would be confirmed and an appendectomy performed. His chief complaints were weakness, a loss in weight of 70 pounds, and stomach trouble. There was no exophthalmos but his metab-

olic rate was plus 79. The symptoms in cases of this type seem to me to be such as would be produced by giving a normal person large doses of thyroid extract.

All the patients in this series who were operated upon have made splendid recoveries, but those who were not operated upon have not responded well to treatment by rest or to other therapeutic measures.

When the glands which were removed in these cases were examined histologically they showed the typical effects of the administration of iodin, for they were all in the colloid resting-state and did not have the markedly hyperplastic appearance which was so frequently seen before we began the preoperative use of Lugol's solution. As Lugol's solution had been used in only about half of these cases, and the histological appearance of all the glands was the same, the logical conclusion is that the glands had been affected by the iodin in the salt.

Another group of cases in which we feel that hyperthyroidism is induced by the use of iodized salt has included elderly women with large adenomata in whom a cardiac breakdown and auricular fibrillation has followed the use of this product. We have seen so many cases of this type that there can be little doubt about the relationship of the iodin to the initiation of the symptoms. That hyperthyroidism is the cause of the cardiac condition in these cases is proved by the basal metabolism estimation and by the improvement that follows operation.

A third group in which extreme sensitivity to iodin is shown includes cases in which hyperthyroidism recurs after operation. Although it is true that cases of recurrent hyperthyroidism have always been seen, formerly they were quite rare. Since the use of iodized salt has become so common, however, they have been seen in increasing numbers; in fact, we saw ten within a period of eight months. In all these cases the return of the symptoms coincided so exactly with the beginning of the use of the salt that there could be no question but that it was the causative factor.

We have seen many other cases of hyperthyroidism besides those of the three types which I have described, in which the patients had been using iodized salt and in which we felt that the symptoms had been caused by its use. In fact, we have found by questioning that of the 2997 patients with hyperthyroidism whom we have seen within the past year and a half, 1174, or 39.17 percent, had been using iodized salt. But since, as I have already said, the etiology of hyperthyroidism is unknown, we do not feel that we have conclusive evidence of the relation of the salt to the disease in all cases.

The use of iodized salt was made general on the supposition that its iodin content was too small to have any detrimental effect. This argument and the excellent results obtained by its use in Switzerland were the chief arguments cited in its support. However, Bircher, (1) a Swiss physician, in a recent article contradicts both assertions. He states that hyperthyroidism has increased 300 percent in Switzerland since the use of iodized

salt has become general and he has observed also that small amounts of iodin administered regularly are more likely to cause iodin poisoning than much larger quantities given periodically. The fact that the incidence of hyperthyroidism has always been very low in Switzerland as compared with the region of the Great Lakes in this country, and the obvious conclusion that the Swiss are much less susceptible to this disease than we, gives this statement event greater weight.

It is interesting to note that since the wave of criticism of this salt has started, the iodin content of salt has been reduced in the state of Ohio from .02 percent to .001 percent on the advice of the State Health Department, although the labeling of the packages still remains the same. I mention this because it seems to me that in spite of statements to the contrary the advocates of this salt have recognized its dangers and have attempted to correct them without seeming to alter their stand in the matter. It would seem to me preferable to correct the evil by having the iodin administered in a more scientific manner and with certain precautions, the chief one being the warning of adults against its use. It is possible that if children are reared on iodin, they will be able to continue its use all their lives without any danger and that in this way goiter will be completely eradicated in a few generations. Certainly no one would wish to discourage a movement which would have such far-reaching, beneficial results. In the meantime, however, it does not seem quite fair that men and women who have reached adult life with, perhaps, an 'iodin starved thyroid gland,' should now be subjected to the danger of having hyperthyroidism induced. It is entirely too easy to contract this disease anyway in this high-strung age!

(1) Bircher, E.: Iodin treatment of goiter, Klin. Wchnschr., 1925, iv, 742-745.

Enlargement and Displacement of the Mediastinum*

By R. H. McDonald, M.D., *Cleveland Clinic. Cleveland, Ohio*

THE mediastinum is that portion of the thoracic cavity which is bounded above by the superior thoracic inlet, below by the diaphragm, posteriorly by the anterior surface of the bodies of the thoracic vertebrae, anteriorly by the posterior surface of the sternum and laterally by the mediastinal reflections of the pleura. It is divided, arbitrarily, into anterior, middle, posterior and superior divisions. The superior division lies above the level of the pericardium and of the other three, the middle division contains the pericardium and heart, while the anterior and posterior divisions are respectively the portions anterior and posterior to the heart and pericardium.

The superior mediastinum contains the arch of the aorta and the vessels arising from it, the innominate veins, the superior vena cava and the thymus gland. It is traversed by the trachea, the esophagus, the thoracic duct, the phrenic and vagus nerves and the sympathetic nerve trunks.

The anterior mediastinum is a very shallow space anteroposteriorly, and very narrow, especially above the point where the two mediastinal pleural reflections meet from the level of the second to that of the fourth costal cartilage. This space contains a small number of lymphatic glands.

The middle mediastinum contains the heart with its attached vessels and part of the root of each lung, the remainder being in the superior mediastinum.

The posterior mediastinum contains the continuation of the esophagus and aorta, the thoracic duct, the azygos veins, the vagus nerves, and the sympathetic trunks. These structures are imbedded in a small amount of loose cellular tissue throughout which are distributed four groups of lymph glands, an anterior mediastinal group, a superior mediastinal group in front of the arch of the aorta and the left innominate vein, a posterior mediastinal group along the aorta and esophagus, and a bronchial group about the bifurcation of the trachea.

The mediastinum thus consists of a more or less elastic set of structures, which are to some extent suspended from above by the trachea, the esophagus, the great vessels and the nerves, but chiefly by the pretracheal layer of the deep cervical fascia, which runs downward on the trachea and common carotid arteries to become continuous with the fibrous layer of the pericardium. Below, the chief attachment of the mediastinum is by the fibrous coat

*Clinical discussion given before the American College of Physicians at the Cleveland Clinic, February 22-25, 1927.

of the pericardium to the central tendon of the diaphragm. The lateral supports are formed by the reflections of the mediastinal to the parietal pleura, anterior and posterior.

The position of these elastic structures is largely determined by two systems of forces. On each side there are intrapulmonic and intrapleural pressures which act as two opposing forces, the former corresponding to atmospheric pressure except for the slight variations which result from respiratory activity, the latter being the result of the elastic recoil of the lung. Normally the intrapulmonic exceeds the intrapleural pressure by from 5 to 10 mm. Hg., and consequently the lung remains dilated; but if this relationship is altered, then the delicate balance of pressure upon the mediastinum is disturbed and in consequence the mediastinum may become displaced.

The elasticity and distensibility of the mediastinum are utilized when the anteroposterior diameter of the thorax is increased in inspiration, but all parts of the mediastinum are equally movable and it never acts as a rigid unit. The most movable structure within the mediastinum is the heart, which is capable of considerable lateral movement within the elastic pericardium.

Clinical methods of investigation will frequently reveal a displacement of the mediastinum; but on account of the anatomical inaccessibility of the area, clinical findings have frequently to be supplemented by laboratory procedures. Symptoms of compression of various structures are useful in the diagnosis of mediastinal tumors, but in a simple displacement there does not occur sufficient alteration of position to interfere with function. Inspection may show that the trachea is deviated to one side, as judged by its relation to the suprasternal notch, and this finding may be confirmed by palpation. Similarly palpation of the apex beat may give some information, although in left-sided displacements one must be certain one is not dealing with a cardiac enlargement.

In percussion of the mediastinum one meets, on the right side, the superior vena cava and the right auricle. On the left side one perceives, from above downward, the first part of the arch of the aorta, the ascending aorta, the left auricular appendage, and the left ventricle. In this connection it is well to remember that the width of the mediastinum in the second interspace, as determined by percussion, depends to a large extent upon the obliquity of the plane of the arch of the aorta in relation to the anteroposterior plane of the body. Dr. Nichols, of this Clinic, has pointed out the many normal variations in the position of the aorta.

Percussion of the heart forms the most reliable guide to the position of the lower mediastinum. Once again one must be sure that enlargement of the heart is not present. Auscultation may reveal the change in position of the maximum intensity of the cardiac sounds. In dextrocardia this maximum intensity will lie to the right of the sternum. Frequently a systolic murmur will be heard over a displaced heart, the displacement of which is due apparently to some alteration in the outline of the mediastinum.

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X-ray examination gives a great deal of information about the position of the mediastinum. In anteroposterior chest plates taken with the same degree of penetration as for the lungs, the trachea should appear in the midline as a streak of greater radiability above the cardiac density. The position of the trachea is a good guide to the position of the superior mediastinum. The position of the heart and its size can readily be seen. In many cases it will be noted that a displacement of the mediastinum is confined to either the upper or lower portions of the mediastinum.

Displacement of the mediastinum implies the presence of a structure which has not lost its normal elasticity. Normally, some loss of elasticity is an accompaniment of increasing age. Pathologically, loss of mobility is caused by the scarring which is an end-result of a local inflammatory process. Chronic mediastinitis will thus result in greater or less immobility but pleuromediastinitis or pleuropericarditis externa is frequently associated with chronic mediastinitis and the resultant contraction of the scar-tissue may cause small lateral displacements.

Unilateral tuberculosis may cause a very considerable displacement of the mediastinum or of some part of it, most notably when the lesion is on the right side. This is the result of pleural adhesions and intrapulmonic cicatrization.

There may be a well marked dextrocardia, in which, however, the apex remains to the left of the base although there is frequently some rotation of the heart in such a way that the apex is pulled away from the chest wall and the base pressed against it. In such cases the visible apex beat disappears from the left side and is replaced by a pulsation at the right of the sternum arising at the base.

A tuberculous process in the upper lobe of either lung may result in a displacement of the upper mediastinum which is evidenced by a lateral position of the trachea. Diagnosis in such a case will be based upon the long history of tuberculosis; the small, contracted, more or less immobile side of the chest, with narrowing of the intercostal spaces; and the intrapulmonic signs.

Other pathological phenomena which cause a displacement of the mediastinum toward the side of the lesion are bronchostenosis, atelectasis and collapse. In bronchostenosis the pulmonary air is absorbed and as a result the lung volume becomes greatly reduced, so that the lung occupies considerably less space within the thorax and the space becomes filled by the increased volume of the other thoracic contents, especially of the other lung.

Displacements of the mediastinum away from the side of the lesion are seen in cases of pneumothorax and of fluid in the pleural cavity. The greatest displacements are seen in cases of spontaneous pneumothorax in young subjects in whom there has been but little inflammatory formation of adhesions. The introduction of air at intrapulmonic pressure into one pleural cavity causes an immediate retraction of the affected lung, provided there are no limiting adhesions; and as the result of the negative pressure in the other side of the thorax, the

mediastinum shifts in an effort to equalize the pressure. Moreover there is frequently a valve action about the site of rupture, so that by the respiratory movements air is actually pumped into the pleural space and high positive pressure results. The history of such a case is one of sudden acute shock with dyspnea. Examination will show the affected side to be full, possibly with widened bulging interspaces, with decreased motion under respiratory activity, tympanitic on percussion at the opposite sternal border, and the typical coin-sound will be heard. Auscultation will show the heart sounds to be absent.

In the case of a simple hydrothorax the fluid in the chest may give rise to marked displacements. In cases of empyema the formation of limiting adhesions is likely to prevent displacement. Hydrothorax is more common on the right side of the thorax in cardiac cases, on account of the pressure of the dilated right auricle on the azygos vein. Displacement of the mediastinum is thus less evident than in cardiac displacements to the right. Examination of the chest will show moderate lack of movement, fullness and dullness on percussion, relative when small amounts of fluid are present and absolute in the presence of large amounts. The outline of this dullness presents the characteristic inverted 'S'-shape, characteristic of fluid in the chest, associated with which is a triangle of dullness posteriorly adjacent to the spine on the opposite side to the fluid, this latter area evidencing the displacement of the posterior mediastinum. Breath sounds over the fluid are diminished, absent, or bronchial in character, depending upon the amount of fluid present.

The mediastinum may be displaced in its upper or lower portion respectively by masses which protrude through the superior thoracic inlet, notably intrathoracic goiter; or by protrusions from below—chiefly diaphragmatic hernia—through the two weak spots of the diaphragm, in the area just posterior to the sternum and around the great vessels.

The suspicion of a diaphragmatic hernia will be aroused by the presence of gurgling sounds in the chest, either the stomach or large bowel being the organ usually involved. Intrathoracic goiter often produces signs of interference with the venous return to the head and upper extremities and the connection of the intrathoracic tumor with the thyroid may be palpable.

In rare instances the mediastinum may be reversed from its normal position. In these cases the heart and thoracic viscera occupy a position and relation which may be described as a mirror image of the normal. Cases in which there is a reversal of only the thoracic cavities are extremely rare, but cases in which there is an associated reversal of the structures throughout the body are much more common. Such a condition was discovered here at the Clinic in the course of the routine examination of a well developed Italian 36 years of age. His history was typical of duodenal ulcer, but otherwise he presented no symptoms. The heart was located in the right chest, the apex beat being palpable and visible in the 6th right interspace, 9 cm. from the midline,

over which the maximum intensity was heard. Examination revealed the major portion of the liver to be located on the left side, and the spleen on the right side. A reversed position of the stomach and colon was revealed by x-ray examination.

Electrocardiographic examination of cases in which there is a rotation of the cardiac axis shows an inversion of all normal waves in lead I. Lead II corresponds to a normal lead III; and lead III corresponds to a normal II.

The Indications for and the Results of the Use of Novasurol, With Reports of Seven Cases*

By H. M. Andison, *Cleveland Clinic, Cleveland, Ohio*

THE value of novasurol as a diuretic of hitherto unprecedented efficiency has come to be recogized during the past seven years. The first account of its use as a diuretic was given by Saxl and Heilig in 1920 and since that time the fact that this drug can overcome edema which has resisted the usual forms of medication has been confirmed by many observers. When used alone it is capable of increasing the output of urine in a most striking manner; but we have found, as have others, that its effect is strikingly enhanced by giving ammonium chlorid at the same time in doses up to 10 gm. per day, and also by restricting the intake of fluids and by the use of a salt-free diet.

Novasurol is the double sodium salt of oxymercurichlor-phenoxyl acetic acid and veronal. It is prepared in a 10 percent neutral sterile solution. This solution contains 33.9 percent of mercury and one cc. contains one gm. of the drug. The drug is administered either intramuscularly or intravenously, but never subcutaneously, because of the resultant irritation of the tissues and the production of sterile abscesses, which heal slowly.

*Clinical discussion given before the American College of Physicians at the Cleveland Clinic, February 22-25, 1927.

Novasurol was first introduced for the treatment of syphilis but for several years it has been used principally as a diuretic. It is indicated in cases of edema due to heart failure; in certain cases of edema of renal origin; in cases of cirrhosis of the liver with ascites; and in cases of carcinoma which involve the liver with resultant ascites. It is of the greatest value in the treatment of edema of cardiac origin and in this Clinic we have used it principally in the treatment of this condition and have secured remarkable results. We have also found it of value in the treatment of two cases of cirrhosis of the liver with ascites. We have not had occasion to use it in the treatment of nephritis.

I am not going to attempt to describe the action of novasurol or the physical and chemical changes which it produces in the blood, in the urine and in the fluid of the edema. It is apparent that it acts both on the kidney and on the extra-renal tissues, but it is the consensus of opinion that the kidneys play the greater rôle in the production of the increased output of urine.

During the past year we have used novasurol in the following groups of cases:—

1. Cases of cardiac failure secondary to hyperthyroidism.... 9

2. Cases of cardiac failure secondary to chronic valvular disease.. 4
3. Cases of cirrhosis of the liver with ascites 2

In all the cases of cardiac edema, without exception, the condition was desperate; there was marked edema of the lower extremities, ascites, moisture in the lungs, and in one case there was a hydrothorax on the right side. In all the cases in which the cardiac failure was secondary to hyperthyroidism, auricular fibrillation was present. In these, the subjective symptoms were marked; the appearance of each patient was characteristic—cyanosis, anxiety, dyspnea and cough. The restlessness and general discomfort were extreme. In fact, each case was of a type the treatment of which by former methods, that is, by the administration of digitalis, of xanthin diuretics and purgation, would have covered weeks and even months. With novasurol, however, the results were striking and were quickly achieved. In some of our cases only one injection was necessary; in others from two to four or five injections of one cc., at intervals of two or three days were required.

The routine management of these cases may be briefly summarized as follows:—

(1) The intake of fluids is restricted to from 800 to 1200 cc. per day.

(2) The diet is free from salt, and contains 40 grams of protein, and about 800 grams of fruit and vegetables, with a total caloric value of 1500 calories.

(3) Digitalization is begun immediately.

(4) Sedatives are given as indicated by the patient's condition.

(5) Ammonium chlorid, gr. 20 to gr. 30 is given by mouth, 4 or 5 times a day.

When ammonium chlorid has been taken for two days and the urine is highly acid, novasurol is given. To test the patient's susceptibility to the drug, a small dose—0.5 cc.—is given at first; if no reaction occurs, one cc. is then injected intravenously. The digitalis and the ammonium chlorid themselves act as diuretics, but do not greatly increase the output of urine. When the novasurol is given, however, there occurs a huge output of urine. This usually begins within three hours of the time of administration of the drug and reaches a maximum in from nine to 12 hours, this maximum effect continuing for 24 hours. Frequently it continues even for 48 hours, but usually the maximum effect is over at the end of 24 hours. The total amount of urine excreted is anywhere from one to four liters and even more. The change in the appearance of the patient is very striking, as the edema becomes greatly, if not almost completely, reduced and coincident with the disappearance of the edema there is a corresponding loss of weight. It is remarkable how rapidly the ascites disappears; how the tense, swollen legs become soft; how the cough is relieved; and how much more comfortable the patient becomes and how grateful he is. The drug is repeated, if necessary, at intervals of two or three days until the edema has completely disappeared. As the heart becomes relieved from its burden, the pulse rate slows and the edema does

not tend to recur. When the edema subsides a more palatable diet is allowed and the fluid intake is gradually increased.

When the ascites is associated with cirrhosis of the liver it is important that the fluid intake should be kept low, and that a diet with a low salt content should be used. Ammonium chlorid is given as in the cardiac cases and novasurol is given at intervals of three or four days or a week. Large doses can be used in these cases. In this way the ascites can be kept in check and paracentesis is not required, or at least, is not as frequently required.

Of particular interest to us has been the value of novasurol in the preparation of thyrocardiac cases for operation. The reduction in the length of time required to prepare the decompensated thyrocardiac patient for operation is something that we have never been able to accomplish before; moreover I believe that this type of preparation not only takes less time, but is more efficient and sure than the methods formerly used. In some of these cases life has been saved for the reason that the heart could be controlled and operation be performed so much earlier. In this group of cases:—One did not come to operation as erysipelas developed and the patient died. In another, post-operative pneumonia developed and caused death. The other seven patients are doing well.

Of the group of cases in which decompensation was due to chronic valvular disease, one patient died of a coronary thrombosis some months afterward, but the edema had not returned. We have not heard from the others.

In our experience we have seen no serious toxic effects following the use of this drug. But symptoms do occur and it is for that reason that we try out the patient's susceptibility with a small dose,—0.5 cc.—before the therapeutic doses are given. Diarrhea is the most common complication we have seen, but it is of no serious consequence and is easily controlled by bismuth and paregoric and a cleansing enema. When giving novasurol it is wise not to give a purgative at the same time, as this increases the tendency to the occurrence of diarrhoea. One of our patients did have a chill and vomiting with no rise in temperature, but this quickly subsided and when the drug was again administered these symptoms did not recur. The ammonium chlorid itself may produce acidosis though this did not occur in any of our cases, as much as 170 grams of ammonium chlorid having been given without any harmful effects. I think that acidosis is more likely to occur in cases of nephritis with a retention of nitrogen, and in these cases the use of novasurol is attended with considerable danger. Should acidosis develop, however, it is readily combatted by the administration of alkalis.

CASE REPORTS

Case I (143844). A woman 27 years of age. The diagnosis was recurrent hyperthyroidism. The patient's heart was markedly enlarged, was fibrillating, and was badly decompensated. Edema was present in the lower extremities and in the abdominal wall. The abdomen was distended with fluid. Breathing was difficult and the patient was very restless. *Treatment*:—restriction of diet and of fluids (1000 cc.); tr. digitalis, 2 cc. every 4 hours; ammonium chlorid by mouth, 20 gr. every 4 hours. The

fluid output was very low. On the third day 1 cc. of novasurol was given, the fluid output on that day was 3790 cc., and by the sixth day the patient had lost 19 pounds in weight. Novasurol was again administered on the eighth day and again there was a very large output of urine. By the tenth day there had been a further loss of 10 pounds and the edema had entirely disappeared. As it had not reappeared by the twenty-first day, a lobectomy was performed. Following the operation the patient had a very severe reaction, pneumonia developed, and death occurred on the fourth day after operation.

Case II (169457). A woman 55 years of age. The diagnosis was very severe hyperthyroidism with secondary myocarditis and acute heart failure. Auricular fibrillation was present, also generalized edema and ascites, and both lungs were full of moist râles. *Treatment*:—restriction of diet and of fluids; tr. digitalis. The pulse became slightly lower and the output of urine was fairly good by the fifth day. The administration of ammonium chlorid was started and on the eighth day 1 cc. of novasurol was given. The urine output for this day was 2160 cc. Novasurol was again administered on the twelfth day, with a resultant output of 2250 cc., and of 2075 cc. on the following day. By this time the patient had lost 28 pounds in weight and was very comfortable. The pulse was about 80, but was still very irregular. Ten days later a lobectomy was performed, the patient stood the operation very well and was discharged on the tenth day after operation. She was last seen four months after the operation, and while her heart was still fibrillating, it was compensated.

Case III (175579). A woman 52 years of age. The diagnosis was very severe hyperthyroidism with secondary myocarditis and acute heart failure. Auricular fibrillation was present, also generalized edema and ascites, and both lungs were full of moist râles. The pulse was 140 and very irregular. On the second day the temperature rose to 104° and there were definite evidences of bronchopneumonia. Treatment for the massive edema seemed to be most urgently indicated, and the following measures were employed: Restriction of diet and of fluids; tr. digitalis; morphia for restlessness; ammonium chlorid by mouth. On the third day 1 cc. of novasurol was given. The output of urine on that day was 2100 cc. Novasurol was again administered on the fifth day, with a resultant fluid output of 4130 cc., and the edema disappeared except for a small amount in the lower extremities. After the third dose of novasurol on the seventh day, which again caused a large output of urine, the edema entirely disappeared. By the tenth day the temperature was normal and the signs of pneumonia had almost entirely disappeared. The pulse was 90, but was very irregular. A week later the edema reappeared. Two doses of novasurol were given, at an interval of two days, and the edema again disappeared. The total loss in weight was 36 pounds. On the twenty-sixth and twenty-eighth days x-ray therapy was applied to the thyroid gland, in order to diminish its activity. The patient was discharged five days following the last treatment, with a normal temperature, pulse 80 but irregular, no edema. She was able to be out of bed and to walk around. She was last heard from one month later and at that time was in fairly good condition, the heart being compensated.

Case IV (161366). A woman 49 years of age. The diagnosis was acute heart failure secondary to hyperthyroidism. The patient was practically *in extremis*, the abdomen being markedly distended by fluid. *Treatment*:—restriction of diet and of fluids (800 cc.); tr. digitalis, 2 cc. every 4 hours; ammonium chlorid, 20 grs. every 4 hours. On the second day 1 cc. of novasurol was given with a resultant fluid output of more than 2000 cc. On the eighth day novasurol was again administered, the fluid output on this day being 2100 cc. and on the following day 1900 cc. As the edema had entirely disappeared and the heart-rate was 90, the ammonium chlorid was discontinued and the fluid intake and the diet were increased. For the next three days the patient was

very comfortable, then her temperature rose sharply to 102.6, and on the following day she had a typical erysipelas of the face. The temperature continued to rise, the erysipelas spread, and death occurred one week after its onset. The edema had not returned and I feel that this patient would have made a good recovery and that operation could safely have been performed had the complication not developed.

Case V (163101). A woman 41 years of age. The diagnosis was hyperthyroidism with secondary myocarditis and cardiac failure. *Treatment*:—Karell diet, tr. digitalis and xanthin as diuretics. No diuresis was produced and the patient's condition did not improve. On the seventh day ammonium chlorid, 20 grs. four times a day, was given, two days later 1 cc. of novasurol was administered intramuscularly, and this was repeated daily for three days, without, however, producing any diuresis. On the fourteenth day 2 cc. of novasurol was given intravenously, with a resultant fluid output of 2800 cc. on that day and of 2075 cc. on the following day. On the next day the novasurol was repeated with a resultant output of 3900 cc. and of 3625 cc. on the following day. The edema had completely disappeared, the patient's condition was improving gradually, and on the thirty-third day after she entered the hospital lobectomy was performed. The patient stood the operation well and left the hospital nine days later. When she returned three months later for the second lobectomy, the heart was again decompensated but not to the same degree as on the previous admission. Ammonium chlorid and novasurol were again employed, with good results, and the second lobectomy was performed 26 days after the patient entered the hospital. She was discharged nine days later and since then has been in fairly good condition. By taking extra precautions her heart has remained compensated.

Case VI (175859). A colored man 58 years of age. The patient complained of having been short of breath for the past six months. The diagnosis was myocarditis, probably luetic in origin, as the Wassermann test gave a finding of 4 plus. The liver was tremendously enlarged, the abdomen was distended with fluid, and edema was present in the whole trunk and in all the extremities, the legs being so swollen that the skin had broken in places. *Treatment*:—special diet; restriction of fluids (800 cc.); ammonium chlorid, 80 gr. per day; novasurol, 1-2 cc. about twice a week. At the end of 25 days the patient had lost 48 pounds in weight and there was only a small amount of edema, this being around the ankles. At this time the patient left the hospital against advice, claiming that he felt so well he did not consider further treatment necessary, and he has not been seen since.

Case VII (176692). A woman 44 years of age. The diagnosis was cirrhosis of the liver. The abdomen had been enlarged for only two months. One week before she entered the hospital the distension had become so great that her physician had performed a paracentesis and had withdrawn about two quarts of fluid. The fluid had collected again very rapidly, and as the patient was very uncomfortable upon admission, paracentesis was again done and 7700 cc. of fluid were withdrawn. *Treatment*:—special diet and restriction of fluids (800 cc.); ammonium chlorid, 80 grs. per day; and novasurol, 1-2 cc., given intravenously every four or five days. The ascites was kept in check by this treatment for a month. At that time it was decided, since the novasurol treatment was such a slow process, to give the patient the small chance offered by the Talma-Morrison operation. This was performed and a drainage tube was left in the wound for 8 days. Twenty-one days after operation the abdomen was so distended with fluid that a drainage tube was again inserted. Seven days later the patient died suddenly. I feel that the patient would have lived quite comfortably and for some time if the more conservative measures had been continued, for the ascites was being controlled very efficiently by the use of novasurol.

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Ocular Disturbances in Diabetes*

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DEFINITE changes are found in the eyes of a large number of patients in whom there is an increased blood-sugar content. One of these changes is functional, the rest are pathological. It is important for the physician to be able to recognize these various changes, not only that he may institute appropriate local treatment but also because of their diagnostic significance.

The only functional disturbance associated with hyperglycohemia is that called *glycosuric amblyopia,* in which the patient has a definite loss of vision without any evident cause. The visual fields show a central loss of color—of red, of green, or of both; they sometimes show a peripheral contraction; and rarely hemianopia (de Schweinitz). Several observers have reported that this type of disturbance is found most frequently in tobacco-users.

As loss of vision, however, may be the only symptom of an increased blood sugar content, it is important to examine the blood in any case of loss of vision of unknown origin. The treatment is confined to treatment of the general condition and to restriction of the use of tobacco, if that is indicated. In these cases the condition is likely to clear up and vision to be restored in great part.

It is not unusual for diabetic patients to have trouble with glasses which have recently been prescribed, or to demand frequent changes. The eye-changes which cause this trouble are usually in the refractive media. Excluding those refractive changes which are due to early cataracts, these changes are of two main types: first, increased far-sightedness, or hyperopia; second, near-sightedness, or myopia.

Cases of the first type have been reported in which the *hyperopia* has attained three diopters. It is thought that this condition is caused by a decrease in the fluid content of the eye, which results in a shortening or a change in the lens itself. Patients suffering from this disturbance usually are relieved by treatment of the diabetic condition, and unless the need is imperative, their glasses should not be changed or new ones supplied until the blood-sugar curve has been fairly stable for a month or longer.

Inability to use the eyes within a range of less than from 18 to 25 inches is often due to *early presbyopia* due to the diabetic condition, for as a rule physiological presbyopia does not appear before the age of 40. This early presbyopia is usually more or less transitory, and if glasses are pre-

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scribed at once they will be too strong after the diabetes has been controlled.

In cases of the second type the myopia is frequently due to a change in the lens similar to that found in the early stages of senile cataract, which results in the so-called 'second sight'. In these cases the lens is probably swollen and unless cataractous changes set in, the difficulty will right itself when the diabetic condition is controlled. The patients in this group frequently have headaches which are not relieved by glasses, because of the instability of the refractive media. For this reason, in any case in which persistent or recurrent headaches are unrelieved by glasses a blood sugar determination should be made.

Weakness or *paralysis* of individual eye-muscles or of groups of them is often a clue to the diagnosis of diabetes. Patients who complain of a sudden ocular disturbance which causes them to see double or to have vertigo should have the various eye-muscles investigated, as they may be completely paralyzed. The muscles supplied by the third nerve are most frequently involved, because the third nerve supplies all but two muscles—the lateral rotator or the external rectus, which is supplied by the sixth nerve; and the superior oblique, which is supplied by the fourth. Whether or not the fourth nerve is affected can be determined by questioning the patient or by employing the various muscle-balance tests. Palsy of the fourth nerve occurs so rarely, however, that it is necessary only to determine whether the third or the sixth is the affected nerve.

Cases of diabetes have been recorded in which there has been a disturbance of accommodation-convergence, that is, an inability to keep an object fused when within reading distance, although it can be seen clearly at this distance with either eye alone.

Ocular muscle palsy is due to diabetes frequently enough to warrant a blood-sugar determination in all cases in which the etiology of the ocular disturbance is unknown. It is not known whether the muscles or the nerve itself is involved in these cases. In the majority of cases the palsy tends to clear up or to improve greatly under general treatment for the diabetes. As for local treatment, the vertigo or diplopia may be relieved by merely pasting a patch over the glass for the offending eye. In cases of long standing the patient learns to suppress one of the images. If the paralysis has been of long duration, surgical intervention may be necessary to give relief.

Diabetic patients sometimes suffer from smarting and burning of the lids, with increased lacrimation and pain on exposure to light (photophobia.) In these cases a lowgrade *conjunctivitis* is sometimes found to be present. Whether this is secondary to a diabetic retinitis or whether it is a separate feature of the diabetes has never been determined. Soothing eye-washes and dark colored lenses frequently give relief.

Discoloration of the skin and of the conjunctiva in association with diabetes is known as *xanthelasma* or *xanthoma*. In a case which we have seen retinal lipemia and xanthelasma were coincident and both conditions cleared up as the diabetic condition

became controlled. Parker quotes Johnson as saying that diabetes may develop in patients who are suffering from xanthelasma.

Iritis is a frequent complication of diabetes. Exudates may appear, and minute hemorrhages may take place, filling the pupillary area and fixing the pupil. It is not unusual for such an iritis to be of a low grade but disastrous to vision (Parker). A thinning or an atrophy of the iris is not uncommon and this may be secondary to the iritis. The symptoms of iritis are inflammation of the eye, pain and photophobia, and sometimes loss of vision. In any case of iritis of uncertain etiology a blood-sugar determination should be made.

An injury of the iris either of accidental or surgical origin in a case of diabetes is often very harmful, as in spite of treatment it may lead to a chronic disturbance with final permanent loss of function and of vision. Fuchs describes a dropsical, bleb-like change in the iris which he claims is due to diabetes.

The cause of the iritis which is associated with diabetes is thought to be an auto-intoxication due to the lowered resistance of the parts, with secondary infection. Good results often follow treatment of the diabetic condition supplemented by local treatment, that is, by putting the eye at rest by keeping the pupil dilated with atropin and by having the patient wear dark glasses. In these cases one must always watch for indications of secondary glaucoma and the patient should be instructed to consult the oculist if any unusual symptoms arise.

Changes in the lens which may accompany diabetes have already been mentioned. These vary from granular or minute deposits to bluish-white 'skimmed milk', radiating streaks. *Cataracts* occur, even in children; in fact, there are four such cases now on record. A diabetic cataract in an adult usually develops more rapidly than the senile cataract. One case was seen at the Cleveland Clinic in which a hazy condition of the lens changed to a complete cataract in a month. In these cases the cataracts are usually bilateral. In these cases there is frequently a very high blood-sugar content, although in the case which we have mentioned the cataract continued to develop while the patient was under treatment and after the blood-sugar level had become normal.

In any case of cataract in a child or in a young adult in which there is neither a history of trauma nor an hereditary factor, diabetes should be suspected. These patients complain of an ever-present mist or veil over their eyes, which they continually attempt to wipe away. If the changes involve the pupillary area the loss of vision is greater than if the periphery of the lens is involved. The changes are posterior-polar or posterior-cortical and are not associated with iridocyclitis (Klein). They are probably due to an alteration in the content of the lens, either an increased sugar content or a lack of nutrition.

The treatment indicated is treatment of the diabetic condition, in the hope of preventing further development of the local disturbance. In some cases the change in the lens may clear up to a certain extent. Surgical treatment

is indicated if the patient is handicapped by his misfortune, but it should be undertaken only after the diabetes is under control. These patients do not always do well, and if one attempts an operation one runs the risk of 'lighting up' an old uveitis or some other focal infection. The success of the operation in these cases depends as much upon the treatment for the diabetes as upon the skill of the surgeon. However, the less trauma that is produced, the better the end-result, for the tissues of diabetics do not react favorably to injury.

Retinitis is frequently associated with diabetes and it usually occurs when the disease is in a late stage. The patient complains of a loss of vision, of photophobia, of floating spots, etc. Examination of the fundus reveals small, punctate, brilliantly white spots, or yellowish-white spots, which are usually discrete, and which sometimes coalesce to form larger patches. They rarely simulate albuminuric retinitis, in which the patches usually form a stellate figure in the macular region. The majority of the punctate spots are in the neighborhood of the central area. There are frequently present minute punctate extravasations of blood which are quite different from the flame-shaped changes associated with nephritis. Vitreous hemorrhages are not uncommon and subhyaloid hemorrhages have been observed.

Wagner and Weder conclude that the primary cause of the retinitis which is associated with diabetes is found in the pathological change which takes place in the vascular system. This view is also held by Cantonnet and others.

A special form of retinitis known as *lipemic retinitis* is sometimes associated with diabetes. At least 28 cases have been reported in the literature (Gray, Root). In these cases the vessels appear to be of equal size and their appearance has been variously described as 'salmon', the 'color of ground glass', 'strawberry and cream', 'waxy', 'creamy', 'milky', or of a 'milky sheen'. The retina is hazy; there is usually little change in the vision; and there are usually no hemorrhages or exudates. This form of eye-change is usually seen in young adults under the age of thirty-five.

The blood shows a high fat content and the urine often contains fat. The fundus-change may be due to an increased amount of fat in the blood, in the adventitia, or in the surrounding tissues. The general prognosis is usually grave; Gray reports a mortality of 57 percent, most of his patients dying in coma. In a case reported by Gray and Root, the patient recovered, and in one seen by the author with John the recovery was complete, with no loss of vision or other defect.

That diabetic patients have retinitis is well known; and that they have retinal changes consisting only of hyperemia, without exudates or hemorrhages and without noticeable vessel-changes, has been noted. Although in many cases vascular changes are present, I do not believe that this entire group should be classified as of vascular origin.

The treatment is directed entirely toward improving the general condition, while as complete ocular rest as possible is prescribed. The prognosis as to vision is poor if the macular re-

gion is involved; the areas involved in exudates become atrophic, and rigid dietary measures and the rest of the usual routine treatment for diabetes offer the only means of relief.

In some cases of diabetes the *optic nerve* is involved in an inflammatory process similar to that seen in acute attacks of the exanthemata or of sinus trouble. The disc shows a haziness with a blurring of the borders; there is increased tortuosity of the vascular system; and not infrequently an associated retinitis. The patient suffers from bright light, and may have a loss of vision. The prognosis is good and general diabetic treatment usually assures relief.

Lowered intra-ocular tension in a case of diabetic coma has been reported by Riesman and Middletown. In the cases which the author has seen in coma the tension, which was measured by the Schiötz tonometer, either showed no change or was increased. In one case, that of a young girl, the tension was 57. This unusual rise may have been due, of course, to the treatment, as the tension was taken shortly after the injection of insulin; however, that was not true in other cases in which also the tension was above normal. In all the cases in which the tension was increased it later became normal.

Parker reports an interesting case of *glaucoma* which failed to respond to surgical treatment, although repeated examinations of the urine showed no sugar, a blood-sugar test showed a content of 250 mg. per 100 cc. The treatment which reduced the blood-sugar content also relieved the ocular condition. The relation of intra-ocular tension to glaucoma is unknown, however this case calls attention to the possibility that diabetes may be a causative factor in some cases of glaucoma.

In conclusion let me call attention once more to the importance of recognizing the ocular disturbances which may be associated with diabetes. When one observes how frequently they occur, one is convinced that all patients who have ocular symptoms or signs the origin of which is unknown should have a blood-sugar test, or better still, a glucose tolerance estimation. It is also important that all diabetic patients with ocular disturbances should have local as well as general treatment, but emphasis should be laid upon the importance of repeated estimations of the blood-sugar content, for it is only by keeping the diabetic condition under control that one can hope to relieve the ocular condition.

Editorial

WITH this issue the Annals begins a new series under a new name "The Annals of Internal Medicine." Many of the members of the College have felt that the old title was too broad, and that "Internal Medicine" should be substituted for "Clinical Medicine" as indicating more precisely the especial field of endeavor of the College. The latter should stand for internal medicine as the American College of Surgeons stands for surgery. This function has not yet been adequately taken up by the College, as the early years of its existence have been so largely given up to organization and establishment on a firm and permanent foundation. This, we believe, has now been accomplished, and the College can now turn its energies actively into taking up for consideration the various problems affecting its especial field. Organized internal medicine has not yet accomplished for the hospital what surgery has been able to do. In consequence it suffers because of its lesser importance in the hospital economy, and as a result its hospital position has not received as complete a standardization as has surgery. The new title will indicate more definitely the function of this association as intended for internists primarily. During the organizing period of the College it has not had full control of its journal either by copyright or financially. This inevitably led to a situation necessitating change. The College must own its journal and have full control of it. The Committee in charge of this problem has fully decided upon this policy, and the College in the future will be the owners and assume the entire responsibility of its publication. In other terms, the College will be the publisher of its Annals. This means for one thing that monthly publication and increased number of pages can be carried out as planned three years ago without too great a cost to the College. The editor will have responsibility only for the material and its prompt publication. A means for more regular publication has been found in the location of editorial office and printer's establishment in the same city, and a new rule as regards proof. The editor's labors have been greatly handicapped by the failure of authors to send in manuscript or to return proof within a reasonable time. It has been almost impossible to secure from those who have presented papers and given addresses at the Clinical Congress copies of these in time for prompt publication. In spite of the rule of the College that all material delivered before it becomes its property for publication in its annals, various invited guests have wholly disregarded this and the College has failed to publish all of the

material offered before its convocations and general meetings. Although a special effort was made to secure a complete publication of everything presented at the Clinical Week in Cleveland, half a dozen or more of the addresses given could not be secured for publication. It is hoped that this situation will be wholly done away with at the New Orleans meeting, and that for the first time the College may be able to publish in complete form all of the material presented in the general meetings. In addition to this it seems also desirable that the most important clinics given during the Clinical Weeks should be put on record in readable form. The work presented to the College at these meetings should be of such a high order that it should deserve a permanent record in the annals of the College. The recording of the Clinical Week, however, is not the only function of the Annals. The editor believes that the College should publish a journal in which valuable contributions from its members not presented at the meetings should have an available opportunity for publication. The Annals should become a record, not only of its meetings but also of the achievements of its members. Articles from the Fellows and Members of the College are therefore solicited by the editor for this journal. The right to go outside of the College for suitable material bearing upon internal medicine will also be exercised by the editor, and he will seek to obtain from leaders in medical research, both in this and in other countries, valuable material of interest to the College. The cultural side of medicine, as well as the scientific and purely clinical, will be represented in these articles. Particularly does the editor hope that the historical side of internal medicine will receive a goodly recognition. The editorial pages will be increased, and it is hoped that the subjects chosen for these will include matters especially interesting to the readers of the journal. The abstract will be chosen for their apparent value, either as dealing with new investigations or summing up old knowledge, whether negative or positive in result. Finally, the reviews will be devoted to new publications especially in the line of internal medicine, but also of general cultural interest relating to medicine. The News Notes will give information concerning the activities of the College and its members. To sum up, the editor hopes that the coming volume for 1927-28 will contain a complete record of the New Orleans meeting, valuable articles on internal medicine by Fellows of the College and others not members of the College, so that it may become a publication regarded as unique in the field of internal medicine, and of value, not only to the members of the College, but to all physicians concerned with the practice of internal medicine. He asks the cooperation of the college in bringing this aim to a successful issue.

Abstracts

Four Cases of Tularaemia (Three Fatal) with Conjunctivitis. H. L. Freese, G. C. Lake and Edward Francis (Public Health Reports, February 26, 1926.)

Tularaemia was demonstrated by animal inoculation and by cultural and serological methods in the sole survivor of an outbreak of a glandular febrile affection with conjunctivitis occurring in four members of a family living in Virginia, three of whom died without tests for tularaemia having been made, either before or after death. The four cases became ill within a 24-hour period and onset was sudden, the father was nauseated, complained of headache and had chills; the three children vomited, and the boy in addition had convulsions. Within 24 hours after the onset, all had axillary temperatures of 103°-104°, conjunctivitis, and swollen lymph glands in the parotid region. There was no skin eruption, and no throat symptoms except some redness. The cervical and axillary glands became much enlarged; there was no evidence of lung involvement and no rigidity or spasticity suggestive of meningitis. All showed the picture of an extreme grade of febrile intoxication. No autopsy was held on any one of the three fatal cases. Swabs taken from the nose and throat of the surviving child and used for rabbit inoculation produced typical tularaemia in six guinea-pigs; and transfers made from these by subcutaneous injection and scarification to 14 others produced death in all with typical lesions of tularaemia, and from these *Bacterium tularense* was isolated in pure culture. The blood serum of the survivor was found to agglutinate *Bac. tularense* in all dilutions from 1:10 to 1:1280 but not in higher dilutions. Although details as to the source and method of infection are wanting, there was abundant proof of contact with rabbits, and the proof of the cause of the illness in the surviving patient justifies the conclusion that all were cases of tularaemia. Whether certain members of the family in dressing infected rabbits transferred the infection by their hands to their conjunctiva, or whether insufficiently cooked rabbit was eaten are matters of conjecture only, but the evidence seemed to point to primary infection of the conjunctiva. It is of further importance to learn that an epidemic had occurred among the rabbits of the neighborhood during the previous May. Tests made in the cooking of infected rabbits proved conclusively that infected rabbits when insufficiently cooked are dangerous as food.

Zur Biologie des Carcinoms. IV Mitteilung. Fritz Silberstein, Johann Freud, Tibor Révész and Blanka Schneid. (Zeitschrift für

die gezamte experimentelle Medizin, April 28, 1927, page 56.)

In February, 1925, these authors reported that they had discovered that experimental mouse tumors were influenced by insulin. This has been confirmed by Műnzen and Rupp, Watermann and von Witzleben; on the contrary Bauer and Nyiri could not confirm their results. The authors have therefore continued their work with the following results. Mice that are being treated with tar-painting for the production of tumors, when treated at the same time with insulin show an inhibition of tumor production. Some of the mice so treated remain tumor free or after a certain time die tumor free, while control animals showed tumors. In the insulin treated tumors the precancerous nodules developed much later than in controls; likewise the malignant transformation of these occurred much later than in controls. The life-duration of the insulin treated animals was much longer than in the controls. In the case of mice that had developed small warts as the result of the tar painting, the further development of these warts was inhibited by protracted insulin treatment, and the duration of life prolonged. When animals belonging to a 100 per cent carcinoma strain were employed for tar painting or inoculated with carcinoma, and treated with insulin, tumor production was inhibited. Some mice remained tumor free; a relatively large number of the mice died tumor free during the treatment, while control animals showed more or less large tumors. In a certain percent of animals the development of the tumor was delayed; in another percentage the tumors after a primary inhibition grew to a large size but were apparently well borne by the animal, the life duration being much longer than in the case of the control animal. The insulin effect was found to be enhanced when certain amounts of dioxyaceton (Oxantin) were combined with the insulin.

Versuche, inoperable Carcinome mit Insulin zu behandeln. FRITZ SILBERSTEIN, JOHANN FREUD and TIBOR RÉVÉSZ. (Zeitschrift für die gesamte experimentelle Medizin, April 28, 1927, page 78.)

On the basis of their experimental work with tar and inoculation carcinoma in mice in which these authors found that a relative immunity could be produced by the administration of insulin, and that this was more striking in animals in which dioxyaceton was given in connection with the insulin, they have applied this treatment to inoperable human cases of carcinoma. Sixteen of these were treated systematically for a long time and fifteen cases for a shorter period. Inasmuch as the majority of cases of carcinoma observed by these workers showed a high degree of insulin tolerance, yet there were some cases that bore only small doses (about 120 units) per day. As a result of their treatments the authors found that the fasting blood-sugar values are above the normal in untreated carcinoma cases. During the course of insulin treatment this value varies. Almost

always periods of increased fasting blood-sugar values occur, followed by a return to normal. When the blood-sugar curves of fasting carcinoma patients and healthy persons are compared certain differences are observable. The first part of the insulin effect in cancer patients is characterized by a slow fall, while the second part is characterized by a rapid rise suggesting that in diabetic cases. The blood sugar values of carcinoma cases rise under the influence of an absolute carbohydrate-free diet, also suggesting the curve in diabetes. This relationship is also demonstrable when insulin is injected shortly before the meal time. Almost all of the cancer patients treated by the authors were in a bad general conditoin. They reacted, with few exceptions, after a few days, with definite improvement of general feeling and increase of strength. It appeared as if insulin treatment kept continually on the border of tolerance inhibited for some time the growth of the tumor and its spread. In one case of uterine cancer the growth remained stationary for over a year. In other cases, during the course of the treatment, a decrease in the size of the tumor and metastases and sharper demarcation were seen. Softening of the tumor masses was produced by direct local injection of the tumor. In the case of accessible tumors moderate doses (60-100 units) were sufficient, that were in general well borne. Injections of larger doses into larger tumors produced no acute hypoglycemic symptoms, but were followed by a condition of intoxication which the authors ascribed to a toxic destruction of albumin, in that it did not respond to a parenteral administration of sugar or to carbohydrate feeding. Sudden breaking off of the insulin treatment was followed by a rapid change for the worse. Gradual cessation of treatment was followed by the same result after some months from the last treatment. The insulin treatment, as in the case of diabetes, must be continuous, or interrupted with great caution and resumed after a not too great interval. The authors believe that insulin treatment in the case of radical operation may be of use in protecting against recurrence and in improving the general symptoms. They recommend also the use of oxantin to increase the action of the insulin, and also that of ergotamin to increase the sympathetic tonus. After systematic insulin treatment a period of maximum tolerance is sooner or later reached; and in these cases in which a direct action upon the tumor was noted, this was coincident with this stage. After long continued insulin treatment the resistance again rises until a record maximum of tolerance is reached.

Reviews

Lectures on Internal Medicine (Delivered in the United States, 1926). By KNUD FABER, M.D., Professor of Internal Medicine, University of Copenhagen, Denmark. 147 pages, 43 figures and charts. Paul B. Hoeber, Inc., New York, 1927. Price in cloth, $3.00.

The four lectures here presented were given during a visit to the United States in February and March, 1926, made under the auspices of the American College of Physicians, the College of Physicians of Philadelphia, the Medical Schools of Baltimore and Boston and the Rockefeller Institute of Medical Research. These lectures were on the following subjects: "The Etiology and Pathogenesis of Achylia Gastrica," "The Intestinal Origin of Pernicious Anemia," "Benign Glycosuria" and "Historical Outline of Medical Therapy, A Sketch." The first of these constituted the Nathan Lewis Hatfield Lecture of the College of Physicians of Philadelphia, February 12, 1926; the second was delivered before the American College of Physicians, February 22, 1926; the third was the Herter Fund Lecture at Baltimore, February 18, 1926; and the fourth was the Harvey Lecture at the New York Academy of Medicine, March 13, 1926. These lectures are beautifully printed in a volume of convenient size. They are original, stimulating and most readable, written in the easy, flowing and distinguished English characteristic of Faber's writings in this language. In the first lecture he maintains his thesis that the very common and important disease called achylia gastrica has nothing particularly remarkable in its etiology and pathogenesis to mark it out from the diseases of other organs; the proper term for the disease is gastritis, by which is to be understood, not the old conception of gastric catarrh, but a disease of the glandular parenchyma of an inflammatory nature. When it is excited through nervous channels, it can only persist for a short time, but apart from this it is due to the same causes which we know produce disease in other organs; direct irritation or hematogenous intoxication by bacterial toxins or autotoxins. The disease is analogous to nephritis and hepatitis, and gastritis should take its place side by side with these diseases. In the second lecture Faber expresses his conviction that pernicious anemia has its origin in intestinal intoxication. Achylia gastrica (anacidity) is the most frequent but not the only cause of idiopathic pernicious anemia. A continually occurring intoxication is the most natural explanation, and in the majority of cases it is an intestinal intoxication by protein toxin. This is the case with Bothriocephalus anemia, stricture anemia, sprue and anemia occurring in patients with achylia. In pregnancy, sepsis and perhaps in syphilis, we must look for the production of toxin elsewhere. The problem of family and hereditary predisposition must be considered in connection with each of these causes. The third lecture is also an interesting compilation of the known facts on benign glycosuria and the glycosuric threshold. Two essentially different forms of glycosuria exist; the first, true diabetes, is due to disease of the islands of Langerhans; the second form of glycosuria is due to deficient blood sugar regulation, and is either due to an habitually abnormally low threshold or an habitually abnormally high alimentary blood sugar rise. In some cases both conditions may be observed. In all of these cases it is, however, a matter of individual constitutional abnormality rather than disease. These abnormalities are harmless to the individual and deserve to be estimated as such by physicians and insurance companies. The practical sig-

nificance of a knowledge of the benign glycosurias cannot be overestimated. Many patients come to be regarded as true diabetics when, in fact, they had only an insignificant passing glycosuria. On account of the extensive occurrence of these non-diabetic forms of glycosuria the correct interpretation of glycosuria is of the very greatest importance to the patient. The question can be determined only by the careful study of the glucose contents of the blood, and we possess the means of doing this in the micro-methods introduced by Bang, and elaborated by Hagedorn and Jensen. The whole development of blood sugar estimation is a fine example of the advantages of exact laboratory analyses. The fourth lecture consists of a sketchy historical outline of medical therapy, and in itself is so interesting that one regrets that Faber did not elaborate this historical study into a volume by itself. It is to be hoped that he may do this later. The development of modern therapy is traced through the periods of "bleeding" pharmacological experimentation, drug-therapy, "Naturheilkunde," hydrotherapy, massage, dietetics, gland-therapy, serum therapy and modern chemotherapy, with the present-day tendency towards "etiotropic remedies," that is, remedies directed towards the specific cause of the disease in the endeavor to effect a really specific and total cure. This last lecture is all too short, and one finishes with the wish that it had been elaborated into a more complete and finished study. The volume is a good example of the class for which Hoeber is becoming noted as a publisher—medical historical studies of prime cultural value, and not mere textbooks. As we have pointed out in other reviews of books issuing from the Hoeber Press, one may find in these productions books that serve particularly well as presentation volumes for physicians and medical students. We take pleasure in recommending this volume of Faber's lectures as the latest addition to this most desirable collection of publications dealing with the cultural side of medicine.

Hypotension. Medicine Monographs, Volume XIII. By ALFRED FRIEDLANDER, Professor of Medicine, College of Medicine, University of Cincinnati. 193 pages. The Williams and Wilkins Company, Baltimore, Maryland, 1927. Price in cloth, gold stamped, 6x9, $2.50.

This volume is the first critical and analytical study of the literature of low blood pressure, and presents a summary of our knowledge on this subject. It will, therefore, be of great interest to practicing physicians and surgeons, life insurance examiners, biologic and physiologic chemists and pharmacologists. The volume begins with an introduction defining low blood pressure in its relationship to health and disease. The clinical methods of estimating blood pressure are given in detail, with a summary of the results of studies of normal blood pressure in the newborn, in childhood and in adult life. Hypotension in apparently healthy whites is then taken up, with a discussion on blood pressure in states of sleep, muscular exercise, relation to body weight, and the factors entering into the maintenance of blood pressure. The various types of hypotension are described. Temporary hypotension in anaphylactic shock, traumatic and surgical shock, relationship of blood pressure to general, local and spinal anesthesia, clinical studies of blood pressure during operations and the treatment of normal and surgical shock are adequately treated; then follow sections on hypotension in acute and chronic diseases and the constitutional diatheses, the relation of hypotension to certain mechanical factors, and the action of tissue and gland extracts and drugs on blood pressure. Pressor and depressor drugs are considered in respect to their blood pressure actions. There follows then an adequate section on essential hypotension, and hypotension due to malfunction of the factors that normally maintain blood pressure: the cardiac factors, the condition of the vessel walls, peripheral resistance and vasomotor tone. Following this there are sections on hypotension in relation to endocrine disorders (adrenals, pituitary gland, gonads, pluri-

glandular disturbances and interglandular associations) with clinical studies, discussion of glandular therapy, endocrine asthenias, present achievements and future prospects of organotherapy. All of these sections contain valuable material, and its assembling in this condensed form makes this volume of great value to the student and practitioner. The volume closes with a general summary and a bibliography of three hundred and seventy-five reading references. This work must be regarded as an essential to be included in any internist's working library.

The Human Body in Pictures. A Visual Text of Anatomy, Physiology and Embryology. By JACOB SARNOFF, M.D., Associate Surgeon, United Israel---Zion Hospital; Attending Surgeon, Harbor Hospital; Consulting Surgeon, Infants' Home; formerly Associate and Instructor of Anatomy, Long Island Medical College, Brooklyn, New York. With Foreword by John Osborn Polak, M.D. 120 pages, and 190 original illustrations, mostly from dissections and animated drawings by the author. Physicians and Surgeons Book Company, Brooklyn, New York. Price in cloth, $2.50.

This is an illustrated teaching manual that follows closely and describes in detail the various anatomical and physiological facts as presented in the motion picture reels and still picture films of "The Human Body Series." These sets can either be purchased outright or rented; the motion pictures are distributed by the Edited Picture System, Inc., New York; and the still picture films by the Bray Screen Products, Inc., of New York. This series of films is intended primarily for students of anatomy and physiology and is especially adapted for use in schools, colleges, nurses' training schools, departments of physical education, etc., to give the lay mind a clear understanding of the essential structures and functions of the human body. For medical students and graduates they may be of use as visual aids in review courses.

College News Notes

Obituaries

Dr. John Reynolds Brown, Tacoma, Washington—May 7, 1927. Heart Disease. Elected a Fellow of The College February 23, 1920.

Dr. Frank Edwin Coulter, Santa Ana, California—July 18, 1927. Coronary Sclerosis. Elected a Fellow of The College February 8, 1921.